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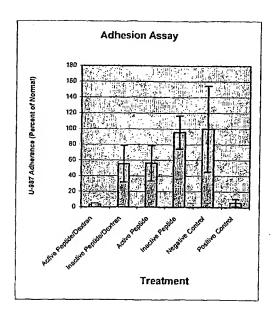
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(54) Title: THERAPEUTIC BIOCONJUGATES



Monocyte adhesion to bovine endothelial cells. All but the positive control were activated with TNF-a to induce ICAM expression. SM1 is the CD11b/CD18 agonist and SM2 is the scrambled, inactive peptide.

(57) Abstract: A therapeutic bioconjugate is composed of a hydrophilic polymer covalently bound to one or more peptides capable of binding specifically to a ligand expressed on a cell surface and thereby forming a biofilm to prevent attachment of cells with the binding partner of the ligand.





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THERAPEUTIC BIOCONJUGATES

CROSS REFERENCE

[0001] This application is a continuation in part of pending U.S. Utility Application, Serial No. 10/295,734, filed November 15, 2002, the disclosure of which is hereby incorporated by reference in its entirety.

FIELD OF THE INVENTION

[0002] The present invention relates generally to biomaterials and, more specifically, to therapeutic conjugates of polymers and peptides capable of binding selectively to ligands expressed on certain cells in target tissues.

SEQUENCE LISTING

[0003] This application also includes a Sequence Listing (158 pages) on paper and on one diskette and two Addenda, all of which are hereby incorporated by reference.

BACKGROUND

Integrins are cell-bound molecules that aid cell-to-cell interactions by providing binding sites for other cells. The integrins are receptors that recognize specific ligands in a variety of physiological and pathological processes. Cellular interactions mediated by the integrins include adhesion, migration, release of soluble factors (cytokines, free radical species, degradative enzymes, etc.), and extracellular matrix (ECM) deposition. These cellular interactions affect pathological processes by reversing them or by sustaining, enhancing or amplifying them.

The integrin superfamily is an important and well characterized group of cell-surface receptors for both cell-substrate and cell-cell adhesion. Integrins are characteristically membrane-spanning heterodimeric protein complexes consisting of a α subunit and a β subunit. Eighteen distinct α subunits and eight distinct β subunits have currently been isolated and identified. While 144 combinations are theoretically possible, 24 $\alpha\beta$ combinations have been observed. Integrin complexes containing the β_1 and β_3 subunits generally are involved in cell adhesion to the extracellular matrix, while the β_2 integrins are involved in cell-cell adhesion.

The complement of integrins expressed by different cell types varies greatly. Depending on the cell type, mammalian cells express from two to ten different integrins, which are the means by which the cell senses its local environment and responds to changes in extracellular matrix composition and topography. Integrins were initially identified as cell-surface adhesion receptors mechanically linking the cell's cytoskeleton to the extracellular matrix or to other cells. Now integrins are also recognized as cell signaling receptors implicated in the regulation of cellular adhesion, migration, tumor metastasis, proliferation, angiogenesis, bone resorption, apoptosis, and gene expression.

[0006] The pivotal importance of integrins in health and disease has lead to a search for therapeutic strategies that target specific receptor-ligand interactions. Research efforts have generally focused on developing antibodies, peptides, and small molecules as therapeutic agents that selectively inhibit these specific receptor/ligand interactions and suppress pathological immune responses. Strategies for pharmacological modulation include blockade of receptors (the application of mAb, soluble ligands, and synthetic ligands); inhibition of expression of adhesion receptors (immunosuppressive and anti-inflammatory drugs, phosphodiesterase and proteosome inhibitors, antisense oligonucleotides); and inhibition of activation of integrins (antagonists of chemokines; anti-inflammatory drugs).

[0007] A threatening pathological condition involving specific receptor-ligand interactions is an excessive inflammatory response. Receptor-ligand interactions are critical for every step of an inflammatory response including neutrophil, monocyte, lymphocyte, and macrophage adhesion to vascular endothelial cells, transvascular migration into inflamed tissues, and phagocytosis of foreign bodies, injured tissues, pathogens, etc. During the inflammatory response, cell signaling releases degradative enzymes and oxidative free radicals to facilitate pathogen and injured tissue removal. Excessive inflammatory response results in the release of these degradative agents at abnormally high levels, damaging healthy tissue.

[0008] One therapeutic approach involves antibodies that are effective in immunomodulation. Researchers have evaluated the effects of post-injury treatment with antibody inhibitors of CD11b/CD18 on pathogenic immune responses. Post-injury treatment with monoclonal antibodies directed against CD11b (integrin α_M subunit) has reduced intestinal ischemia/reperfusion-mediated lung and liver injury without affecting levels of circulating and sequestered PMNs. Monoclonal antibody directed against CD18 (integrin β_2 subunit) has

effectively reduced intestinal ischemia/reperfusion-mediated tissue injury in vivo. Preclinical studies have also shown that anti-ICAM-1 and anti-CD11b/CD18 therapies can increase tolerance (decrease rejection) in several transplantation models including cardiac, cornea, skin, pancreatic islet, and peripheral nerve allografts.

[0009] In another approach, antisense oligonucleotides, blocking ICAM-1 expression in donor and host tissues, are being developed to limit reperfusion injury and decrease allograft rejection rates for heart and kidney transplant.

[0010] However, the current therapeutic regimens against CD11b/CD18 are limited to local delivery because systemic delivery would lead to a globally impaired immune system. Delivery systems and reagents that selectively target and block cell adhesion to prevent pathological inflammation have been sought.

[0011] The repertoire of leukocyte types and receptor-ligand interaction described for inflammatory responses are also involved in autoimmune diseases [rheumatoid arthritis (RA), multiple sclerosis (MS), Graves disease, Crohn's disease (CD), AIDS, diabetes, graft-versus-host disease (GVHD), inflammatory bowel disease (IBD)] and rejection of allograft tissues/organs.

[0012] Autoimmune and allograft rejection responses are distinguished by the recruitment of T-cells and the development of a specific/adaptive immune response. Integrin interactions with ligands play a key role in recruiting circulating T-cells to extravascular sites where autoimmune and allograft rejection occurs. In the case of T-cells, extravascular infiltration is critical for antigen recognition, clonal expansion of specific antigen-responsive T-cells, and the destructive attack of cytotoxic T-cells on antigen-bearing tissues. These specific receptor-ligand interactions represent therapeutic targets for suppressing pathologic adaptive immune responses, and therapeutic strategies have been sought to modify receptor-ligand interactions in therapy of autoimmune diseases and allograft rejection.

[0013] New reagents and methods for treating and preventing excessive inflammation, autoimmune diseases, tissue rejection, cancer metastasis and other pathological conditions preceded by the binding of an integrin receptor with its ligand are being sought.

BRIEF DESCRIPTION OF THE FIGURES

[0014] FIG 1 schematically represents the anti-inflammatory/immunosuppressant action of the bioconjugates of the present invention. The normal immune response to vascular injury

and the response of the injured site in the presence of the biospecific bioconjugates are illustrated. The diagram shows the biointerface formed by the bioconjugates of the present invention creating a physical barrier against subsequent inflammatory cell adhesion.

[0015] FIG 2 is a reaction scheme for the preparation of a preferred embodiment of the present invention, a dextran-peptide bioconjugate.

[0016] FIG 3 is a nuclear magnetic resonance representation of dextran.

[0017] FIG 4 illustrates the results of an adhesion assay of a bioconjugate of the present invention with bovine endothelial cells stimulated to express the integrin ligand ICAM-1. In this assay, the bioconjugate effectively bound to endothelial cells, reducing monocyte adhesion to levels observed in control, non-stimulated cells.

SUMMARY

[0018] Bioconjugates capable of preventing cellular interactions mediated by integrin/ligand binding have been discovered. When administered to an individual, the bioconjugates form a cell adhesion barrier in a target tissue that prevents and treats the pathological conditions preceded by cellular interactions. The bioconjugates comprise a hydrophilic polymer and a peptide wherein the peptide preferably comprises at least the binding site of an integrin for a ligand expressed on a cell. When applied to a living tissue, the bioconjugates bind specifically to cells expressing the ligand and form a blockade or biofilm that prevents subsequent cell binding at the blocked tissue. Pathological consequences of cellular interactions, which include inflammation, autoimmune diseases, tissue rejection, cancer metastasis and other pathological conditions preceded by cellular interactions, are thus prevented.

[0019] The therapeutic bioconjugate includes a hydrophilic polymer; and one or more peptides capable of binding specifically to a ligand expressed on a cell surface. The bioconjugate blocks interactions between cells in a living tissue when the ligand is expressed on the surface of at least one of said cells. Moreover, the bioconjugate can block interaction between a cell and an extracellular matrix wherein said ligand is capable of binding to a component of said matrix. The bioconjugate is intended to block pathological reactions triggered by cellular interactions in a living tissue.

In some embodiments, the bioconjugate has a peptide that includes the amino acid sequence of the binding portion of an integrin for a tissue-bound ligand. The bioconjugate may have blocking cell signaling receptors implicated in the regulation of cellular adhesion, migration, tumor metastasis, proliferation, angiogenesis, bone resorption, apoptosis, or gene expression. Among these are the binding portion of an integrin α subunit or an integrin β subunit. These binding portions of the integrin subunits include SEQ ID NOS 1-202. The bioconjugate's binding portion can be, for example, a portion of the integrin α_2 subunit (CD49b, VLA-2, platelet gpla) I domain, integrin α_4 (CD49b, VLA-4), integrin α_5 (CD49e, VLA-5), integrin α_L (CD11a) I domain, integrin α_M subunit (CD11b) I domain, integrin α_{IIb} I domain, integrin α_{IIb} (CD41) heavy chain, integrin α_{11b} (CD41) light chain, integrin β_1 (CD29) subunit, the integrin β_2 (CD18) subunit, integrin β_3 (CD61) subunit, or integrin β_7 (LPAM-1) subunit.

In one embodiment, the bioconjugate's peptide includes the portion of the integrin [0021] α₂ subunit (CD49b, VLA-2, platelet gpla) I domain that binds specifically to ligands CN I, CN II, CN III, CN IV, LN and/or the echovirus-1 receptor. In another embodiment, the bioconjugate's peptide is a portion of the integrin α_4 (CD49b, VLA-4) subunit that binds specifically to the ligands VCAM-1, FN, MAdCAM-1, TSP and/or invasin. In yet another embodiment, the bioconjugate's peptide is a portion of the integrin α_5 (CD49e, VLA-5) that binds specifically to ligands FN, L1 or invasin. In other embodiments, the bioconjugate's peptide is a portion of the integrin α_1 (CD11a) I domain that binds specifically to the ligands ICAM-1, ICAM-2. ICAM-3 or LPS. In other embodiments, the bioconjugate's peptide is a portion of the integrin α_M subunit (CD11b) I domain that binds specifically to the ligands iC3b, ICAM-1, ICAM-2, ICAM-4. Fb. Factor X, CD23, NIF, heparin, beta glucan, or LPS. In other embodiments, the bioconjugate's peptide is a portion of the integrin α_{11b} (CD41) heavy chain that binds specifically to the ligands Fb, FN, VN, TSP or vWF. In other embodiments, the bioconjugate's peptide is a portion of the integrin α_{11b} (CD41) light chain that binds specifically to the ligands Fb, FN, VN, TSP and vWF. In another embodiment, the bioconjugate's peptide is a portion of the integrin β₁ (CD29) subunit that binds specifically to the ligands FN, LN, CN, VCAM-1, FN, MAdCAM-1, TSP or invasin. Moreover, the bioconjugate's peptide can be a portion of the integrin β₂ (CD18) subunit that binds specifically to the ligands ICAM-1, ICAM-2, ICAM-3, ICAM-4, LPS, iC3b, Fb. Factor X, CD23, NIF, heparin, and/or betaglucan. In another embodiment, the bioconjugate's

peptide is a portion of the integrin β_3 (CD61) subunit that binds specifically to ligands fibrinogen, fibronectin, vitronectin, thrombospondin, von Willebrand factor, osteopontin, bone sialoprotein, laminins, collagens, and/or neural cell adhesion molecule L1.

[0022] In another embodiment, the bioconjugate's peptide is a portion of the integrin β_7 (LPAM-1) subunit that binds specifically to the ligands VCAM-1, fibronectin, MAdCAM-1, or E-cadherin (cadherin-1).

[0023] This invention also includes the nucleic acids coding for peptides of the peptide portion of the bioconjugates. The nucleic acid sequences are provided in SEQ ID NOS 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 86, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 186, 185, 187, 189, 191, 193, 195, 1197, 199 and 201.

This invention also includes the peptides for preparation of bioconjugate having their sequence set out in P-2, P-49 and SEQ ID NOS 1-218 and modified with an additional N-terminal or C-terminal cysteine residue. In another embodiment, the above nucleic acid sequences are modified to accommodate the additional cysteine residue(s).

[0025] The bioconjugates also include a polymer, that can be a polysaccharide or an oligosaccharide. In another embodiment, the polymer is derived from a polysaccharide or an oligosaccharide by the addition of chemical groups capable of reacting with a peptide to form said bioconjugate.

In another embodiment, the bioconjugate has the formula XY_b wherein X is a low cell-adhesive, hydrophilic polymer, Y is a peptide comprising a portion of the binding site of an integrin for a ligand expressed on a cell surface, and b is greater than b. In another embodiment, the polymer b is a polysaccharide or an oligosaccharide. In another embodiment b is a derivative of a polysaccharide or of an oligosaccharide in which the derivative saccharide has reactive groups such that the derivative saccharide reacts with peptides to form the bioconjugate. The reactive group can be a hydroxyl group. In other embodiments, the polysaccharide or oligosaccharide can be agarose, dextran, heparin, chondroitin sulfate, hydroxyethyl starch, and hyaluronic acid. More preferably, the polymer is a dextran and thed peptide is the binding portion of an integrin. In other embodiments, the polymer is polyvalent and is, for example,

poly(ethylene glycol), poly(ethylene oxide), poly(vinyl alcohol), poly(acrylic acid), poly(ethylene-co-vinyl alcohol), poly(vinyl pyrrolidone), poly(ethyloxazoline), and/or poly(ethylene oxide)-co-poly(propylene oxide) block copolymers. In other embodiments, the polymer can be copolymers, block copolymers, graft copolymers, alternating copolymers, or random copolymers. Preferably, the polymer is essentially inert. Preferably, the polymer is degradable by hydrolytic or enzymatic means. Examples of degradable polymer are one or more blocks consisting of lactic acid, glycolic acid, ε-caprolactone, lactic-co-glycolic acid oligomers, trimethylene carbonate, anhydrides, and amino acids. In one embodiment, the polymer is a serum protein, such as albumin

[0027] In other embodiments, the bioconjugate is in a pharmaceutically acceptable carrier. Alternatively, the bioconjugate is immobilized on a solid substrate. Preferably, the bioconjugate is immobilized on an implantable medical device. The bioconjugate could be immobilized on a drug delivery device or an *in vitro* diagnostic device.

[0028] In other embodiments, there is provided a kit including one or more bioconjugates as well as reagents and apparatus suitable for administering the bioconjugate to an individual. Alternatively, the bioconjugate can be in a pharmaceutically acceptable carrier.

[0029] In one embodiment, there is formed on a mammalian tissue a biointerface such that the biointerface includes a plurality of bioconjugates bound to a plurality of ligands on the tissue.

There also is provided a method of preparing a bioconjugate including the steps of providing a hydrophilic polymer having one or more reactive groups, providing a bioselective peptide comprising a chemical group capable of reacting with the reactive groups, and contacting the polymer and the peptide under conditions such that the reactive and chemical groups react to form the bioconjugate. In another embodiment, the reactive groups of the polymer are hydroxyl groups and the chemical group of the peptide is a sulfhydryl group. In preferred embodiments, the polymer is a polysaccharide, such as activated dextran or hydroxyl starch.

[0031] In other embodiments the peptide of the bioconjugate is selected from the group consisting of SEQ ID NOS 7-14, 25-32, 35-38, 43-48, 55-56, 65, 66, 93, 94, 97, 98, 107-110, 119-124, 133-136,141, 142, 153, 154, 157-164, 171-174, 179-200, 203-212, 215 and 216, the peptide comprising a cysteine residue. In other embodiments, the peptide is selected from the

group consisting of SEQ ID NOS 1-218, the peptide including additionally an N-terminal or a C-terminal cysteine residue.

[0032] In other embodiments, there is provided a method of preparing a bioconjugate including the steps of providing a peptide selected from the group consisting of SEQ ID NOS 1-218, modifying the peptide by addition of an N-terminal or C-terminal cysteine residue, providing an amount of activated dextran, and contacting the activated dextran and the modified peptide under conditions, whereby the dextran and the modified peptide react to form the bioconjugate.

[0033] There is also provided a method for preventing adhesion of a mobile cell to a cell immobilized on a substrate including the step of applying a bioconjugate specific for the immobilized cell under such conditions that the bioconjugate forms a cell adhesion barrier on the immobilized cell and prevents adhesion of the mobile cell.

There also is provided a method of blocking pathological reactions triggered by cellular interactions in a living tissue. This method has the step of administering to the living tissue a bioconjugate selective for a target tissue, whereby the bioconjugate forms a cell adhesion barrier at a targeted tissue site. In other embodiments, the bioconjugate is the binding portion of an integrin for its ligand expressed on the target tissue. In other embodiments, the bioconjugate is administered intravascularly, orally, intramuscularly, intraperitoneally, subcutaneously, cerebrospinally, endovascularly, rectally or topically. When the bioconjugate is administered intravascularly in a biologically compatible solution, it is administered at a concentration of between about 1 μg/L and 100 g/L. Preferably the bioconjugate is administered to an individual in a pharmaceutically acceptable composition. Preferably, the amount of administered bioconjugate is between about 1-1000 mg/kg body weight.

[0035] In another method of preventing and treating thrombosis, an anti-coagulating amount of a bioconjugate having one or more peptides capable of binding selectively to integrin ligands expressed on inflamed endovascular cells is administered to tissue containing the inflamed endovascular cells. In other embodiments, the integrin ligands are CN I-IV, LN, or the Echovirus-1 receptor. In other embodiments, the bioconjugate's peptide is selected from the group consisting of P-2, P-49, and SEQ ID NOS 1, 2, 3-8, 91-106, 129-192, 203 and 204.

[0036] Also provided is a method of preventing and treating atherosclerosis. An antiatherosclerotic-effective amount of the bioconjugate including one or more peptides capable of binding selectively to integrin ligands expressed on or around atherosclerotic cells is administered to tissue containing the atherosclerotic cells. In other embodiments, the integrin ligands are VCAM-1, FN, MAdCAM-1, TSP, invasin or a combination thereof. In other embodiments, the bioconjugate's peptide is selected from the group consisting of P-49 and SEQ ID NOS 9-38, 59-106, 129-202 and 207-210.

[0037] Also provided is a method of Claim 57 for preventing and treating systemic inflammatory response syndrome. An effective amount of the bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands expressed on cells in such inflamed tissue is administered to the tissue. In other embodiments, the integrin ligands are FN, L1 or invasin. The bioconjugate's peptide(s) is selected from the group consisting of P-49 and SEQ ID NOS 9-38, 59-106, 129-202 and 207-210.

[0038] In the method of preventing and treating multiple organ failure (MOF), a MOF-effective amount of the bioconjugate having one or more peptides capable of binding selectively to integrin ligands expressed on cells in affected tissue is administered to the tissue. In other embodiments, the integrin ligands are ICAM-1, ICAM-2, ICAM-3, LPS or a combination thereof. The bioconjugate's peptide(s) is selected from the group consisting of P-49 and SEQ ID NOS 39-58, 107-128 and 211-218.

In the method of preventing and treating autoimmune disease, an effective amount of a bioconjugate including one or more peptides capable of binding selectively to integrin ligands expressed on cells implicated in the autoimmune disease is administered to tissue containing the cells. In other embodiments, the integrin ligand is VCAM-1, FN, MAdCAM-1, TSP, invasin, ICAM-1, ICAM-2, ICAM-3, LPS, iC3b, ICAM-1, ICAM-2, ICAM-4, Fb, Factor X, CD23, NIF, heparin, β-glucan, LPS, FN, Fb, CN I, VN, FN, LN, CN, Fb, Factor X, CD23, NIF, heparin, β-glucan or a combination thereof. The bioconjugate's peptide(s) are selected from the group consisting of P-2, P-49 and SEQ ID NOS 1-218.

[0040] In the method of preventing and treating inflammatory diseases, an effective amount of a bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands expressed on cells of inflamed tissue is administered to a tissue containing the inflamed cells. The integrin ligand may be CN I-IV, LN, Echovirus-1 receptor, VCAM-1, FN, MAdCAM-1, TSP, Invasin, L1, LPS, ICAM-1-4, iC3b, Fb, Factor X, CD23, NIF, heparin, β-

glucan, VN, vWF or a combination thereof. The bioconjugate's peptide(s) is selected from the group consisting of P-2, P-49, and SEQ ID NOS 1-202 and 205-219.

[0041] In a method of preventing and treating allograft transplant rejection, an anti-rejection amount of a bioconjugate having one or more peptides capable of binding selectively to integrin ligands expressed on T cells implicated in allograft transplant rejection is administered to an individual having transplanted tissue. The integrin ligand may be VCAM-1, FN, MAdCAM-1, TSP, invasin, ICAM-1-4, LPS, iC3b, Fb, Factor X, CD23, NIF, heparin, β-glucan, LN, CN, vWF, OP, BSP, L1 and E-cadherin. The bioconjugate's peptide(s) may be any of P-49 and SEQ ID NOS 9-30, 39-58, 91-200 and 211-218. Transplant rejection also may be concurrently treated with an Immunosuppressant, such as cyclosporine.

In a method of preventing and treating Crohn's disease, an effective amount of the bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands expressed on inflamed cells in gut tissue is administered. The integrin ligand may be VCAM-1, FN, MAdCAM-1, TSP, invasin, ICAM-1-4, iC3b, Fb, Factor X, CD23, NIF, heparin, β-glucan, CN I, VN, LN, OP, BSP, L1, vWF and/or E-cadherin. The bioconjugate may have one or more peptides selected from the group consisting of P-49 and SEQ ID NOS 9-30, 30-58, 93-200 and 211-218.

[0043] In a method of preventing and treating inflammatory bowel disease, an effective amount of a bioconjugate includes one or more peptides capable of binding selectively to integrin ligands expressed on inflamed cells in gut tissue is administered. The bioconjugate has one or more peptides selected from the group consisting of P-49 and SEQ ID NOS 9-30, 39-58, 91-200 and 21-218.

[0044] In a method of preventing and treating sequelae of a bacterial infection, an effective amount of the bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands expressed on secretory membranes is administered. The bioconjugate has one or more peptides selected from the group consisting of P-49 and SEQ ID NOS 39-58, 107-192 and 211-216.

[0045] In a method of preventing and treating sepsis or septic shock, an effective amount of a bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands such as LFA-1, ICAM-1, VCAM-1 and a combination thereof is administered. The

bioconjugate includes one or more peptides selected from the group consisting of P2, P-49 and SEQ ID NOS 1-30, 39-58, 91-200 and 211-18.

[0046] In a method of preventing and treating ischemia-reperfusion injury, an effective amount of a bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands is administered intravenously. The bioconjugate includes one or more peptides selected from the group consisting of P-49 and SEQ ID NOS 9-30 and 39-218.

[0047] In a method of preventing and treating cancer metastasis, an anti-metastasis effective amount of the bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands is administered systemically to an individual or locally to tissue containing or suspected of containing cancer. The bioconjugate includes one or more peptides selected from the group consisting of P-49 and SEQ ID NOS 91, 92, 203 and 204.

[0048] In a method of treating conditions caused by viper and rattlesnake bites, an anti-venom-effective amount of the bioconjugate having one or more peptides capable of binding selectively to at least one integrin ligand on a bitten tissue site is administered. In some embodiments, the bioconjugate has a peptide of SEQ ID NOS 153 and 154.

[0049] Also embodied herein are therapeutic replacement fluids including a bioconjugate and a pharmaceutically acceptable diluent.

DETAILS OF THE INVENTION

[0050] We have created a family of bioselective bioconjugates that specifically bind to ligands expressed during cell-cell interactions including immune responses that result in pathology. The bioconjugates selectively target and bind to tissue surfaces, forming a protective barrier against pathologically driven cell-cell interactions. The bioconjugates, provided systemically or locally, selectively target tissues to suppress pathologically excessive damage to healthy tissues and thus limit deleterious outcomes. The various bioconjugates may be used in the prevention and therapy of a number of pathological processes involving leukocyte adhesion to tissue surfaces, including but not limited to, inflammation, septic shock, post-trauma multiple organ failure, ischemic reperfusion injury, transplant rejection, infectious inflammatory diseases, and autoimmune diseases. Other pathological responses that are the result of cell-cell interactions that may be therapeutically treated by the present bioconjugates include, but are not

limited to, thrombosis, atherosclerosis, cancer metastasis, autoimmune diseases, hookworm infection, bacterial and viral infection, and the sequelae of viper and rattlesnake bites.

[0051] The term "bioconjugate" as used herein means a compound in which at least two components, a peptide and a cell-adhesion-barrier polymer are chemically attached, i.e., conjugated. Methods of conjugation of the bioselective peptide and the cell adhesion barrier molecules are generally known in the art. The specific conjugation method is determined by the choice of cell adhesion barrier molecule and the accepted linking methods to the selected bioselective molecule, preferably a protein or peptide. Both univalent and multivalent conjugation methods are suitable. The conjugation method is selected to produce a bioconjugate that retains the bioselective and blockade abilities of the bioconjugate. In preferred embodiments of the invention, the molecules are attached *in vitro* prior to application to the living tissue. In certain other embodiments the molecules may be designed with appropriate linking groups that cause them to congregate *in vivo*.

As used herein "bioselective" means a molecule that (a) is capable of binding specifically to its ligand, preferably an integrin ligand; (b) is physiologically compatible with living tissue; (c) is generally chemically inert; and (d) exhibits little or no binding affinity for cellular components other than the targeted ligand. Peptides having the amino acid sequence based on the ligand binding site of the integrins have a selective affinity for the targeted ligand, e.g., provide the targeting ability of the bioconjugates for tissue such as injured or diseased tissue that express the ligand. Since normal tissue does not generally express these ligands (or expresses ligand in low quantity), the bioselective bioconjugates may be delivered systemically as well as locally as therapeutic agents to suppress inflammation where these ligands are expressed and to prevent the pathological consequences of excessive tissue inflammation.

[0053] As used herein, the term "integrin ligand" means the moiety on a specific cell type that binds to surface-bound integrins during the course of cellular interactions. Integrin ligands are the target binding site for the bioconjugates of the present invention. Each bioconjugate comprises one or more peptides that bind specifically to one or more particular cell-surface expressed ligands and also comprises a low-adhesive polymer. The bound bioconjugates block binding at the ligand to any subsequent cell surface integrin by forming a blockade or an "internal tissue bandage" that prevents specific, unwanted cell-cell interactions.

[0054] The term "peptide" is used herein in its broadest sense to refer to a sequence of subunit amino acids, amino acid analogs, or peptidomimetics. Peptides may be linked, for example, by peptide bonds, to form polypeptides.

[0055] The term "biointerface" as used herein means a collection of bioconjugates of the present invention bound to their ligand on a cell surface. When a bioconjugate binds to its ligand, an essentially inert blockade results, and subsequent interaction between cells is prevented.

[0056] The term "cell adhesion" as used herein means the binding of at least one cell to another cell or to a component of an extracellular matrix.

[0057] The term "cell adhesion barrier" as used herein means the biointerface that forms in situ in a tissue as a result of bioconjugate binding. Cell adhesion barrier molecules have properties that intrinsically inhibit cell adhesion by forming a physical barrier to cell-cell/tissue adhesion when applied to cell, tissue, or biomaterial surfaces. The cell adhesion barrier prevents adhesion of circulating cells to a cell surface, a component of an extracellular matrix or another material.

The term "polyvalent polymer" as used herein means a polymer having more than one reactive group at which a peptide or other moiety may be chemically linked to the polymer. In preferred embodiments of this invention, the reactive groups are hydroxyl groups that react with the sulfydryl groups on a peptide to form the bioconjugate. The polyvalency of the polymer provides the opportunity to make a bioconjugate comprising multiple connections of a peptide to the polymer or multiple peptides, which may be the same or different.

[0059] The therapeutic bioconjugates of the present invention comprise a polymer that forms the cell adhesion barrier. Preferably the polymer is multivalent, i.e., contains multiple reactive groups to allow a high number of peptides to be incorporated into the bioconjugate. In certain preferred embodiments, the polymer component is a hydrophilic polymer that is highly soluble in aqueous solutions.

[0060] The therapeutic bioconjugates of the present invention also comprise one or more peptides that selectively and strongly bind cell ligands and effectively immobilize the polymeric component at a tissue surface. Tissue ligands are typically in high enough concentrations on tissue surfaces to promote high-density surface binding of bioconjugates, creating a polymer

barrier to cell adhesion on ligand-presenting surfaces. The polymeric barrier is a biointerface on a tissue surface that blocks subsequent binding of circulating cells to the tissue surface.

The therapeutic bioconjugates of the present invention can be prepared from readily available starting materials using the following general methods and procedures. It will be appreciated that where typical or preferred process conditions (i.e., reaction temperatures, times, mole ratios of reactants, solvents, pressures, etc.) are given, other process conditions can also be used unless otherwise stated. Optimum reaction conditions may vary with the particular reactants or solvent used, but such conditions can be determined by one skilled in the art by routine optimization procedures.

[0062] The bioconjugates are preferably prepared by contacting a cell-adhesion-barrier polymer having multiple reactive chemical groups with a peptide having multiple chemical reactive groups under conditions where the polymer and peptide react to form covalent bonds.

[0063] Disclosed herein is a method for synthesis of a preferred embodiment of the present invention, bioconjugates comprising dextran and one or more peptides having the amino acid sequence of a portion of the integrin binding site. In a preferred method, dextran containing multiple hydroxyl groups is reacted directly with peptide functional groups (usually SH or S-S) to form covalently bound peptide in the dextran bioconjugate. Generally, the reaction is conducted at a temperature and a time such that (1) the solvent is in liquid form, (2) the dextran and the peptide do not degrade, and (3) detectable levels of product is obtained. Preferably, this reaction is conducted in the presence of a suitable solvent, e.g., water, under atmospheric conditions and pH optimal for formation. Upon completion of the reaction, the resulting bioconjugate of activated dextran and covalently attached peptide is recovered by conventional methods including, but not limited to, neutralization, extraction, precipitation, chromatography, filtration and the like.

[0064] Another preferred method for preparing the bioconjugates is presented. In this method a polymer having multiple reactive chemical groups is contacted with linker molecules containing two or more chemical reactive groups under conditions whereby the two compounds react to form covalent bonds. The polymer with covalently bound linker molecules is then contacted with a peptide with multiple chemical reactive groups under conditions whereby the two components react to form covalent bonds and the final therapeutic bioconjugate product.

[0065] Also disclosed is a method for synthesis of a preferred embodiment of the present invention, bioconjugates comprising dextran and one or more peptides having the amino acid sequence of the binding site of an integrin. In this method, dextran is first activated by reaction with a linking molecule, preferably dimethylaminopyridinine (DMAP). Generally, this reaction is conducted at a temperature and time range such that (1) the solvent is in liquid form, (2) the cell adhesion barrier polymer, (3) the linking molecule do not degrade, and (4) detectable levels of product are obtained. Preferably, the reaction is conducted in the presence of a suitable solvent, e.g., DMSO, under atmospheric conditions optimal for product formation. completion of the reaction, the resulting conjugate containing the cell adhesion barrier polymer with covalently attached linking molecules, e.g., activated dextran, is recovered by conventional methods such as neutralization, extraction, precipitation, chromatography, filtration and the like. The multiple functional groups of activated dextran react with a sulfhydryl group, preferably on a cysteine residue in the peptide. Upon completion of the reaction, the resulting bioconjugate containing dextran with covalently attached peptide is recovered by conventional methods including, but not limited to, neutralization, extraction, precipitation, chromatography, filtration and the like.

Peptides are presented that may be used in the synthesis of the present bioconjugates. The peptides preferably comprise the amino acid sequence of the binding site of an integrin specific for a targeted ligand expressed on a cell surface. The peptides also comprise one or more sulfhydryl groups provided, generally, by cysteine residues. Certain of the peptides comprising amino acid sequences of binding sites of the integrins naturally comprise cysteine. Other preferred peptides may be modified for use in the synthetic methods by the addition of N-terminal or C-terminal cysteine residues. Preferred peptides for use in the preparative methods of the present method are members of the group consisting of SEQ ID NOS 1-112, with a cysteine residue added to the N- or C-terminus of peptide sequences which do not naturally have cysteine. The peptides described herein may be isolated from a naturally occurring protein, may be chemically synthesized, or may be recombinantly expressed by methods well known in the art. Nucleic acids for recombinant preparation of the peptides are presented in SEQ ID NOS 113-225.

[0067] Table 1 (at end) presents the amino acid sequence of the peptides, the nucleic acid sequence corresponding to each peptide, the integrin from which the peptide is derived, the target

ligand for each peptide and therapeutic administration of the preferred bioconjugates of the present invention.

From Table 1 it can be seen that the bioconjugates of the present invention may be used therapeutically in a large number of diseases and disease states caused by pathological consequences of cell-cell interactions through integrin/ligand binding. Many of these diseases involve inflammation at various tissue sites as, for example, Crohn's disease, intestinal bowel disease, multiple organ failure (MOF), systemic inflammatory response, and septic shock. Other diseases that are the pathological consequences of intercellular reactions mediated by integrins and may be therapeutically treated by the bioconjugates of the present invention include, but are not limited to allograft transplant rejection, cancer metastasis, bacterial or viral infection, thrombosis, atherosclerosis, ischemia-reperfusion injury, autoimmune diseases, and hookworm infection.

[0069] The above table is a compendium of known integrin/ligand pairs and illustrates the therapeutic applications of bioconjugates comprising these known integrins. However, it is anticipated that as new integrins are discovered and characterized, they may likewise be used as sources of peptides in the bioconjugates of the present invention and will find therapeutic use in preventing and treating disease states in which integrin/ligand binding is implicated.

[0070] In certain embodiments of the present invention, peptides other than those derived from integrins may be used to form cell adhesion barriers. Thus, for example, bioconjugates synthesized from a barrier polymer and antibodies or antibody fragments capable of binding to selected antigens expressed on a cell surface, an extracellular matrix or tissue surface may likewise be used in the methods of the present invention to prevent or treat diseases triggered by cellular interactions.

[0071] The therapeutic bioconjugates of the present invention bind to a specific target tissue. This specificity is achieved by selecting the peptide component of the bioconjugate that specifically binds to ligands that are expressed on cells in selected tissues, not generally on cells circulating in the bloodstream. A bioconjugate capable of binding to circulating cells might create aggregates in the bloodstream which could compromise blood flow. Examples of ligands expressed on non-circulating-cell surfaces include, but are not limited to, CN I, CN II, CN III, CN IV, LN, Echovirus-1 receptor, VCA, FN, L1, invasin, MAdCAM-1, TSP, ICAM-1, ICAM-2, ICAM-3, ICAM-4, iC3b, Fb, Factor X, CD23, NIF, heparin, β-glucan, LPS, VN, vWF, FN, LN,

CN, VCAM-1 and MAdCAM-1. The definition of these abbreviations are given at the end of Table 1.

[0072] In an important aspect of the present invention, pharmaceutical compositions comprising one or more bioconjugates of the present invention and a pharmaceutically acceptable carrier are presented. The pharmaceutical combinations and methods of this invention are adapted to therapeutic use as agents in the treatment or prevention of pathological excessive leukocyte adhesion/infiltration and subsequent tissue injury according to the methods described herein. The bioconjugates may be suspended in aqueous solution, e.g., saline solution, for intravenous delivery of the therapeutic compounds.

[0073] The compounds of the present invention are generally administered in the form of a pharmaceutical composition comprising at least one of the bioconjugates of this invention together with a pharmaceutically acceptable carrier or diluent. Thus, the compounds of this invention can be administered either individually or together in any conventional oral, or parenteral dosage form.

[0074] For oral administration the pharmaceutical composition can take the form of solutions, suspensions, tablets, pills, capsules, powders, and the like. Tablets containing various excipients such as sodium citrate, calcium carbonate and calcium phosphate are employed along with various disintegrants such as starch and preferably potato or tapioca starch and certain complex silicates, together with binding agents such as polyvinylpyrrolidone, sucrose, gelatin and acacia. Additionally, lubricating agents such as magnesium stearate, sodium lauryl sulfate and talc are often very useful for tabletting purposes. Fillers in soft and hard-filled gelatin capsules have preferred materials, including lactose or milk sugar as well as high molecular weight polyethylene glycols. When aqueous suspensions and/or elixirs are desired for oral administration, the bioconjugates of this invention can be combined with various sweetening agents, flavoring agents, coloring agents, emulsifying agents and/or suspending agents, as well as such diluents as water, ethanol, propylene glycol, glycerin and combinations thereof.

[0075] The bioconjugates of this invention may also be administered in a controlled release formulation such as a slow release or a fast release formulation. Such controlled release dosage formulations of the combination of this invention may be prepared using methods well known to those skilled in the art. The method of preferred administration will be determined by

the attendant physician or other person skilled in the art after an evaluation of the subject's condition and requirements.

[0076] For purposes of parenteral administration, solutions in sesame or peanut oil or in aqueous propylene glycol can be employed, as well as sterile aqueous solutions of the water-soluble salts and sugars. Such aqueous solutions may be suitably buffered, if necessary, and the liquid diluent first rendered isotonic with sufficient saline or dextrose. These aqueous solutions are especially suitable for intravenous, intramuscular, subcutaneous and intraperitoneal injection. In this connection, the sterile aqueous solutions are all readily obtainable by standard techniques well known to those skilled in the art.

[0077] Methods of preparing various pharmaceutical compositions with a certain amount of active ingredient are known, or will be apparent in light of this disclosure, to those skilled in this art.

[0078] The present invention also relates to pharmaceutical compositions in kit form. The kit may include one or more pharmaceutical compositions. The kit includes container means for containing the compositions. Typically the kit includes directions for the administration of the compositions. The kit form is particularly advantageous when the separate components are administered in different dosage forms (e.g., oral and parenteral) or are administered at different dosage concentrations as desired by the prescribing physician.

[0079] In an important aspect of the present invention, improved biomedical devices are presented. The devices are improved by the incorporation of one or more bioconjugates of the present invention disposed on or in the biomedical device.

As used herein, a "biomedical device" refers to a device to be implanted into or attached to a tissue in a subject, for example, a human being, in order to bring about a desired result. Particularly preferred improved biomedical devices according to this aspect of the invention include, but are not limited to catheters coated with the present bioconjugates to prevent localized inflammation around the biodevice. Similarly, wound dressings are biomedical devices that may be improved by coating with the present bioconjugates and then applied to inflamed surfaces.

[0081] As used herein, "disposed on or in" means that the one or more bioselective bioconjugates can be either directly or indirectly in contact with an outer surface, an inner surface, or embedded within the biomedical device. "Direct" contact refers to disposition of the

bioconjugates directly on or in the device, including, but not limited to, soaking a biomedical device in a solution containing the one or more bioconjugates, spin coating or spraying a solution containing the one or more bioconjugates onto the device, implanting a device that would deliver the bioconjugate, and administering the bioconjugate through a catheter directly on to the surface or into any organ or transplant.

[0082] "Indirect" contact means that the one or more bioconjugates do not directly contact the biomedical device. For example, the one or more bioconjugates may be disposed in a matrix, such as a gel matrix or a viscous fluid, which in turn is disposed on the biomedical device. Such matrices can be prepared to, for example, modify the binding and release properties of the one or more bioconjugates as required.

Exact dosing of bioconjugate therapy depends on many factors, among them the [0083] binding affinity of a particular bioconjugate for the targeted tissue ligands and the rate at which the bioconjugate is cleared from targeted tissue sites. Binding affinity of the bioconjugate for tissue ligands affects the amount of local tissue requirements for maintaining saturated coverage of bioconjugate on ligand-expressing tissue. Two major factors affect binding affinity: 1) the number of ligand-binding peptides per conjugate molecule; and 2) the affinity of the complexed peptide for the targeted ligand. The rate at which the bioconjugate is cleared from targeted tissue sites is dependent in part on the turnover rate of cells presenting tissue ligands. The turnover rate is driven by a constant internalization of surface molecules, and ligand internalization rate determines the duration of the ligand-bound bioconjugates on cell/tissue surfaces. The amount of bioconjugate delivered to a particular tissue in an individual in need of therapy varies by size of person, affinity of the peptide of the bioconjugate for the target ligand, turn-over rate of cells at the specific stage of disease at the time of administration and the mode of administration. It is anticipated that continuous or multiple administrations of bioconjugate will be most effective in treating and controlling the progress of disease.

[0084] In an important aspect of the present invention, methods are given for treating diseases caused by the pathological reactions triggered by interaction between different cell types in a living tissue. The methods comprise the step of administering to a subject in need thereof an amount of a bioselective bioconjugate of the present invention effective to block target ligands and thereby suppress subsequent cell-cell interaction and prevent the diseases.

[0085] In the methods of the present invention, the therapeutic bioselective bioconjugates may be administered by targeted delivery or by localized delivery. As used herein "targeted delivery" means systemic delivery of the present bioconjugates to an internal inflamed tissue surface. The biospecific bioconjugates target tissue surfaces with selected ligands and thus are agents of targeted delivery.

As used herein "localized delivery" means, for example, the direct application of the present bioconjugates to an exposed tissue surface. Topical application to a wound or inflamed burned tissue, for example, would be most suitable for localized delivery. Delivery systems such as aerosols or swabs may be used in localized delivery to other tissue or mucosal surfaces. Intra-arterial delivery of bioconjugate to a particular organ also is contemplated.

Therapy of inflammation in tissue

[0087] It has been discovered that the normal response to vascular injury may be suppressed by certain therapeutic bioconjugates that selectively target and locally bind to inflamed tissue surfaces that express certain ligands, such as ICAM-1. The bound bioconjugates form a protective barrier against abnormally excessive leukocyte adhesion/infiltration and subsequent tissue injury. The effective blockade suppresses the pathological consequences of excessive leukocyte adhesion/infiltration into vulnerable tissue.

[0088] To exemplify the biospecific activity and adhesion of the bioconjugates of the present invention, the characteristics of a preferred embodiment, the dextran/ICAM-1-binding A domain peptide conjugates, to inflammatory cells were measured as described in Experiments 2 and 3 hereinbelow.

endothelial cells expressing ICAM-1. In FIG 1, the intravascular action of the present bioconjugates is illustrated. In FIG 1, the lumen of the vessel and circulating blood/fluid volume are illustrated above the endothelial layer; the vessel wall is below the endothelium. FIG 1 (A) illustrates a normal blood vessel in uninjured tissues with circulating polymorphic neutrophils (PMNs). FIG 1 (B) illustrates inflamed (ICAM-1-expressing) endothelial cells following tissue injury. PMNs bind to ICAM-1 on inflamed endothelial cells and invade the vessel wall and surrounding tissues. Traumatic shock can induce excessive PMN adhesion and activation resulting in damage to healthy tissues and multiple organ failure (MOF). FIG 1 (C) illustrates

an inflamed blood vessel immediately after infusion of resuscitative fluids containing dextran/ICAM-1-binding peptide bioconjugate of the present invention. FIG 1 (D) illustrates binding of dextran bioconjugate to inflamed endothelial cells forming a non-adhesive barrier to PMNs. Invasion of PMNs into healthy tissues is thus reduced. Other leukocytes that interact with ICAM-1 are also blocked by this therapeutic strategy. Other endothelial cell surface ligands, e.g., VCAM-1, could also be targeted using peptides that selectively bind to other endothelial cell surface ligands.

[0090] Methods are presented for suppressing inflammation in a tissue. In certain instances, an inflamed tissue is contacted locally with one or more bioconjugates in an amount effective to inhibit tissue/leukocyte binding and suppress inflammation. The topical methods may also be used to enhance healing of inflamed flesh wounds caused by trauma or heat. In other instances the bioselective bioconjugates are delivered systemically to target the inflamed tissue sites. These methods are useful for preventing and treating inflammatory diseases including chronic inflammation of gut, cervix, eyes and lung.

[0091] In preferred methods for preventing and treating inflammatory diseases, an anti-inflammation-effective amount of a bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands expressed on tissues containing the inflamed cells is applied to inflamed tissue such as such as gut, cervix, eyes, lung and inflamed flesh wounds. In these methods the bioconjugate comprises peptides capable of binding to the target ligands expressed on inflamed tissue cells. Most preferably the bioconjugate comprises one or more peptides selected from the group consisting of P6-P16, P21-P30, P48-P104, P109-P112 (Table 1).

[0092] In preferred methods for preventing and treating systemic inflammatory response syndrome (SIRS), there is administered an anti-SIRS-effective amount of bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands expressed on cells in inflamed tissue. Preferably, the bioconjugate comprises peptides capable of binding to a target ligand from the group shown in Table 1. Most preferably the bioconjugate comprises one or more peptides selected from the group consisting of P1-99, P104 and P106-112 (Table 1).

[0093] In preferred methods for preventing and treating inflammatory bowel disease (IBD), an anti-IBD-effective amount of bioconjugate comprising one or more peptides capable of binding selectively to target ligands expressed on cells in inflamed bowel tissue is applied to

the tissue. Preferably, the bioconjugate comprises peptides capable of binding to an integrin ligand from the group shown in Table 1. Most preferably the bioconjugate comprises one or more peptides selected from the group consisting of P6-P16, P21-P30, P48-P104 and P109-P112 (Table 1).

In preferred methods for preventing and treating Crohn's disease (CD), there is administered an anti-CD-effective amount of bioconjugate comprising one or more peptides capable of binding selectively to target ligands expressed on cells in inflamed bowel tissue. Preferably, the bioconjugate comprises peptides capable of binding to the target ligand from the group shown in Table 1. Most preferably the bioconjugate comprises one or more peptides selected from the group consisting of P6-P16, P21-P30, P48-P104 and P109-112 (Table 1). The nucleotide sequences are provided in Table 2.

The utility of the compounds of the present invention as medical agents in the prevention and suppression of inflammatory cell responses to vulnerable tissue and as a therapeutic agent to prevent the pathological consequences of excessive inflammation in mammals (e.g., humans) is demonstrated by the activity of the compounds of this invention in cell adhesion assays described below in Examples 2 and 3.

Therapy of disorders due to pathogenic immune responses

[0096] In a further aspect, the invention provides methods for treating or inhibiting a disorder due to pathogenic immune responses. Although leukocyte adhesion to tissue surfaces is essential for normal immune system function, leukocyte/tissue adhesion plays a major role in a number of pathological processes including septic shock, post-trauma multiple organ failure, ischemic reperfusion injury, transplant rejection, inflammatory diseases, and autoimmune diseases. Accordingly, these methods provide targeted therapeutics for these diseases.

Topical and systemic anti-inflammatory/immunosuppressant therapeutic methods are presented for treating and preventing leukocyte adhesion/infiltration, to suppress inflammation and to prevent the pathological processes that result from excess inflammation. Integrin-mediated leukocyte/tissue adhesion plays a major role in a number of these pathological processes.

[0098] Methods for treating and preventing ischemia-reperfusion injury are provided. In the methods an anti-ischemia-reperfusion-injury-effective amount of a bioconjugate comprising one or more peptides capable of binding selectively to target ligands expressed on endothelium is administered intravenously. In the methods the bioconjugate comprises peptides capable of binding to the target ligand. Most preferably the peptides may be selected from the group consisting of P6-P16, P21-P104 and P106-P112 (Table 1).

Therapy and prevention of infection by pathological agents

[0099] Methods are presented for preventing or treating pathogenic immune responses resulting from infection by bacteria, a biological warfare agent, anthrax or small pox, for example. Sexually transmitted diseases caused by bacterial pathogens or viral pathogens may likewise be prevented and treated. In these methods an effective immunosuppressive amount of a bioselective bioconjugate of the present invention is administered to an individual in need thereof.

[0100] Methods are presented for treatment of septic shock resulting from bacterial infection. Many bacteria (including agents of biological warfare, like anthrax) not only invade and infect host organisms, but also release endotoxins that promote a massive, systemic inflammatory response, resulting in an immune attack on healthy as well as diseased tissue. The present method protects tissues against injurious pathogenic immune responses. In certain instances the therapeutic method is used in adjunct with antibiotics to increase patient/casualty survival.

[0101] Infections of many types can result in hypersensitivity reactions, which are typically treated with steroids such as hydrocortisone and prednisolone, which have the drawback of side effects and interference with clearing the parasite (bacterial, viral or ameboid). Examples include SARS-related pulmonary hypersensitivity and hookworm infestation. In pulmonary infections, inflammatory exudates form in alveoli and bronchi and are organized by extensive matrix deposits and scarring. Ligands for integrins include CN III and CN IV.

[0102] Pancreatic infection results in damage to the ducts (epithelial cells), periductal inflammation, and new extracellular matrix expansion. Collagen also may be present and attract integrin-expressing cells.

[0103] In an important aspect, methods are presented for treatment of septic shock resulting from bacterial infection. Many bacteria (including agents of biological warfare like anthrax) not only invade and infect host organisms but also release endotoxins that promote a

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massive and systemic inflammatory response resulting in an immune attack on healthy as well as diseased tissue. Among the abnormalities is deposition of platelets on damaged epithelium. The present method protects tissues against injurious pathogenic immune responses. In certain instances the therapeutic method is used in adjunct with antibiotics to increase patient/casualty survival.

[0104] In methods for preventing and treating septic shock, an anti-septic shock effective amount of a bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands expressed on endothelium. The product must be infused intravenously. Preferably, the bioconjugate comprises one or more peptides selected from the group consisting of P1-P16, P21-P30, P48-P102, P109-P110 (Table 1).

Therapy of post-trauma multiple organ failure

[0105] Methods are presented to prevent and treat post trauma multiple organ failure. A bioselective bioconjugate of the present invention in a resuscitative fluid for preventing post-trauma multiple organ failure is presented.

[0106] Severe trauma can invoke a massive and systemic inflammatory response resulting in an immune attack on healthy as well as diseased tissue. The present methods may be used to protect tissues against injurious pathogenic immune responses that promote multiple organ failure. In this aspect, methods are presented for preventing the pathogenic results of intestinal ischemia and reperfusion that promote leukosequestration and injury in the gut as well as other organs resulting in multiple organ failure (MOF). Polymorphonuclear neutrophils (PMNs) play a key role in MOF since they respond to injury by adhering to tissues in multiple organs and releasing injurious oxidative agents.

[0107] In methods for preventing and treating multiple organ failure (MOF), an anti-MOF-effective amount of a bioconjugate comprising one or more peptides capable of binding selectively to target ligands expressed on endothelial cells. Preferably the bioconjugate comprises one or more peptides selected from the group consisting of P1-16, P21-104 and P106-P112 (Table 1).

Treatment of wound trauma

In these embodiments, the bioselective bioconjugates may be incorporated into blood replacements that are shipped in a dry or lyophilized formulation in conventional fluid therapy bags or are otherwise added to the conventional fluids.

[0109] Targeted and localized protection from pathogenic immune responses triggered by diseases that cause ischemic injury (injury due to lack of oxygen), e.g., heart attack and stroke, are also presented.

Prevention of transplant rejection

[0110] In another aspect of the invention, methods are presented for locally suppressing transplant rejection of allograft organ transplants including heart, lung, liver, kidney, skin, pancreatic islets, and cornea. In these methods biospecific bioconjugates target ICAM-1 on organ transplants, reducing or eliminating inflammation and the need for traditional systemic immunosuppression therapy, which is less specific.

Prevention and treatment of autoimmune disease.

[0111] Also presented are targeted and localized methods for protection from autoimmune diseases, including, but not limited to, diabetes and rheumatoid arthritis. At least ICAM-1 and LFA-1 are implicated in autoimmune diseases. Blocking those receptors is a

strategy for blocking autoimmune reactions and limiting conditions such as diabetes and rheumatoid arthritis. MAdCAM-1 receptors also have been implicated in diabetes.

Prevention of atherosclerosis

[0112] Atherosclerosis is an inflammatory condition. Endothelium is injured by a variety of sources (e.evated cholesterol, hypertension, etc.) and begins to display receptors that are ligands for integrins. The receptors include but are not limited to ICAM-1, VCAM-1 (vascular cell adhesion molecule) and PDGF.

Treatment and Prevention of Cirrhosis

[0113] Cirrhosis is the replacement of hepatocytes with fibrotic cells and is due to an inflammatory processes such as hepatitis and toxic reactions. Ligands for integrins also are present in cirrhosis. These include collagen I and III (CN I and CN III).

Treatment and Preventions of Glomerulosclerosis

[0114] This disorder is characterized by inflammatory destruction of renal glomeruli and replacement by fibrotic scar tissue. Such pathology is associated with the presence of CN I, CN IV and fibrinogen, which serve as ligands for integrins.

Prevention of Cancer Metastasis

Tumor metastasis is a fine-tuned balance between the formation and loosening of adhesive cell contacts within the tumor, which is regulated by various integrins. For example, human ovarian cancer cells express integrin $\alpha_{\nu}\beta_{3}$, which associates with vitronectin in the extracellular matrix and correlates with cancer progression. Exposure of such cancer cells to vitronectin results in proliferation and motility increase of five fold. Once blood-borne metastatic cancer cells may lodge in the lungs, causing early, intravascular metastatic tumors. Pulmonary vasculature contains integrin ligands known as calcium-activated chloride channels (CLCA) which are specific for the specific-determining loop (SDL) of β_{4} . Two mechanisms of fighting cancer metastasis are blocking vitronectin with the ligand-binding portion of $\alpha_{\nu}\beta_{3}$ and

blocking the CLCA ligand with a peptide including amino acids (SEQ ID NOS 184-203) of integrin β_4 .

Sequelae of Viper and Rattlesnake Bites

[0116] Snake bites may cause excessive capillary permeability, which may be mediated by integrins.

Examples

Example 1

[0117] This experiment presents the synthesis of a preferred embodiment of the present invention, an anti-inflammatory dextran/peptide bioconjugate. This reaction scheme is illustrated in FIG 2.

Synthesis and chemical characterization of methacroylated dextran

[0118] Dextran, molecular weight about 70kD (25 g), and dimethylaminopyridinine (DMAP) (5 g) were dissolved in dimethylsulfoxide (DMSO) (225 ml) under nitrogen atmosphere at room temperature. Glycidyl methacrylate (GMA), a linking molecule, was added to the mixture to produce GMA-derivatized dextran (dex-GMA). The amount of GMA was adjusted to obtain 10 degrees of substitution (DS) (DS: molar ratio of GMA per glucopyranose residue). The reaction was terminated after 48 hours. The product was purified from the reaction mixture by solvent removal and size exclusion chromatography. Aqueous solutions of methacroylated dextran were rapidly frozen in liquid nitrogen, lyophilized, and stored frozen. FIG 2 illustrates the chemical structures of dextran, GMA, and methacroylated dextran and the dextran-peptide bioconjugate. FIG 3 is an NMR of dextran.

Synthesis of the anti-inflammatory dextran/peptide bioconjugate by coupling a synthetic peptide (CNAFKILVVITDGEK) to activated dextran

[0119] The synthetic peptide was based on the portion of integrin $\alpha_m\beta_2$ (CD11b/CD18) that fits in the ICAM-1-binding pocket. Synthesis with this peptide is illustrative and other peptides may likewise be coupled to dextran or other polyvalent polymers. The synthetic peptide (CNAFKILVVITDGEK) was added to phosphate buffered saline (PBS) with 1.5 mM EDTA at a final concentration of 20 mM. The pH was adjusted to 8.0-8.5 with triethanolamine (TEA). Methacroylated dextran (2mM) was then added to the reaction mixture and the pH was adjusted

again to pH 8.0-8.5 with TEA. All solutions were maintained under inert conditions to minimize disulfide bond formation. Crosslinking was allowed to proceed at room temperature for two hours. The reaction mixture was then dialyzed against deionized water in 25,000 MWCO membrane to remove any unreacted or disulfide-bonded peptide. The purified dextran/peptide conjugates were recovered by lyophilization.

A bioconjugate containing an inactive scrambled sequence of the above A-domain peptide CTVDLKFGIKNIEAV, was similarly synthesized and was conjugated to dextran and used as the sham control in the *in vitro* assays described below. Synthetic peptides were added to phosphate buffered saline (PBS) with 1.5 mM EDTA at a final concentration of 20 mM. The pH was adjusted to 8.0-8.5 with TEA. Methacroylated dextran (2mM) was then added to the reaction mix and the pH was adjusted again to pH 8.0-8.5 with TEA. All solutions were maintained under inert conditions to minimize disulfide bond formation. Crosslinking was allowed to proceed at room temperature for two hours. The reaction mixture was then dialyzed against deionized water in 25,000 MWCO membrane to remove any unreacted or disulfide-bonded peptide. The purified dextran/peptide conjugates were recovered by lyophilization.

Example 2

This experiment illustrates the activity of the bioconjugate, whose synthesis was described above, in the inflammatory cell adhesion assay. Bovine endothelial cell (BEC) monolayers were established in 24-well culture dishes. At 24h prior to the assay, normal medium (Minimal Eagle's Medium with 10% fetal bovine serum, 1% ABAM and 1% L-glutamine) (Gibco, CA, USA) was replaced with medium containing tumor necrosis factor α (TNF- α , 10 ng/ml). Following the 24h incubation period, each sample well received a medium change.

[0122] Treated sample groups received medium containing 6% dextran bioconjugate or 6% bioconjugate. Negative control samples received medium containing dextran bioconjugate whose peptide had a scrambled A domain sequence. Two other control treatments were given: a medium change with no dextran or peptide was given to a sample group pretreated with TNF-α, and a positive control that was not pretreated with TNF-α. After a 30-minute incubation period, the medium in all wells was replaced with medium containing the human monocyte cell line U937 (1 x 10⁵/ml) (ATCC, Manassas, VA). All samples were incubated for another 30 minutes,

then washed three times with PBS to remove non-adherent cells. The average number of adherent cells per 100x microscopic field was determined for each sample group.

Referring to FIG 4, the results of this assay illustrate the biospecific binding of the peptide/dextran conjugate to bovine endothelial cells. In this assay all but the positive control were activated with TNF-α to induce ICAM expression. The negative control represents 100%. Treatment with active peptide conjugate resulted in a relative monocyte adherence of 3.34±1.69%. The positive control, where the endothelial cells were not induced, had monocyte adherence of 5.741±4.81%, which is not statistically different from samples where ICAM expression was induced preceding treatment with the active conjugate. The treatment with the inactive peptide conjugate yielded a relative adherence of 55.65±23.42%, while treatment with the active peptide alone led to a monocyte adherence of 56.28±22.67%. The treatment with the inactive peptide alone was comparable to no treatment after the TNF-α activation. Inactive peptide treatment gave a relative monocyte adherence of 95.71±21.03%. The standard deviation for the negative control was 54.5.

The active dextran bioconjugate effectively bound to TNF- α stimulated, ICAM-expressing BECs and prevented monocyte adhesion to the extent observed in non-stimulated BECS (positive control). Unconjugated peptides, dextran, and the inactive peptide conjugate inhibited cell adhesion poorly, suggesting that only the combined effect of specific binding of active peptide conjugates to ICAM and formation of an ICAM-bound nonadhesive dextran layer promoted reduced monocyte adhesion to TNF- α stimulated, ICAM-expressing BECs. Since leukocyte/tissue adhesion plays a major role in a number of the pathological processes discussed above, these bioconjugates could be utilized as targeted therapeutics for many applications.

Example 3

[0125] This experiment illustrates the inhibition of leukocyte/inflamed cell binding in human umbilical vein endothelial cell (HUVEC) monolayers by the bioselective bioconjugates of the present invention.

[0126] To assess the effect of these peptide-dextran bioconjugates on inflammatory cell adhesion, the following *in vitro* ICAM-1-mediated leukocyte cell adhesion assay was performed. HUVEC monolayers were established in 24-well culture dishes. At 24h prior to the assay,

normal culture media were replaced with medium containing TNF- α (10 ng/ml). Following the 24h incubation period, each sample well received a medium change. Treated sample groups received medium containing 6% dextran bioconjugate (dextran conjugated to the A domain peptide CNAFKILVVITDGEK). Untreated control samples received normal medium. Negative sham control samples received medium containing dextran conjugate with a scrambled A domain sequence (KCENGADFTKIIVLV). All samples were then incubated for 30 min prior to the adhesion assay. Medium was removed from all wells following the 30 min incubation and replaced with medium containing U937 monocytic cells (1 x 10^5 /ml). All samples were then incubated for another 30 min. After this incubation period, samples were washed three times with PBS to remove non-adherent monocytes. The samples were then fixed, and an average number of adherent monocytes per 100x microscopic field was determined for each sample group. Statistical comparisons between sample groups (n = 4 replicate wells per group) were performed using a student's t-test.

[0127] U937 cell adhesion to inflammatory HUVECs was reduced by 87.7% in the sample group treated with bioconjugate containing the active A-domain sequence CNAFKILVVITDGEK. No significant reductions in cell adhesion were observed in untreated and sham-treated (scrambled A domain peptide conjugated to dextran) sample groups.

[0128] It should be understood that the invention is not limited to the particular embodiments described herein, but that various changes and modifications may be made without departing from the spirit and scope of this novel concept as defined by the following claims. The following references are incorporated by reference.

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ADDENDUM A

TABLE 1 – NUCLEOTIDE SEQUENCES

TABLE 1 – NUCLEOTIDE SEQUENCES

			<u></u>			
SEQ ID #	ID#	Nucleotide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
1	D-1	ACT TAC AAA ACA AAG GAG GAA ATG ATA GTA GCA ACG AGT CAG ACC AGT CAA TAT	Integrin α ₂ subunit (CD49b, VLA-2, platelet gpIa) I domain	CN I-IV, LN, Echovirus-1 receptor	Thromb, Ather, SIRS, MOF, SS, ID	1
NA	D-2	ACT TAC AAA	Integrin α ₂ subunit (CD49b, VLA-2, platelet gpIa) I domain	CN I-IV, LN, Echovirus-1 receptor	Thromb, Ather, SIRS, MOF, SS, ID	2
3	D-3	CAG ACC AGT CAA TAT	Integrin α ₂ subunit (CD49b, VLA-2, platelet gpla) I domain	CN I-IV, LN, Echovirus-1 receptor	Thromb, Ather, SIRS, MOF, SS, ID	2
5	D-4	ATA GCA GTA ATA GGA	Integrin α ₂ subunit (CD49b, VLA-2, platelet gpla) I domain	CN I-IV, LN, Echovirus-1 receptor	Thromb, Ather, SIRS, MOF, SS, ID	3
7	D-5	AAT TTC CTA GAG AAG TTT GTT CAG GGT CTC GAT ATC GGC CCT ACC AAA ACC CAG GTC GGT CTG ATA CAA TAT GCG AAT AAT CCA CGC TGG TTC AAT CTA AAT ACT TAT AAG ACT AAG GAA GAG ATG ATT GTT GCT ACC TCC CAG ACT AGC CAG TAC GGC GGT GAT CTA ACA AAT ACA TTC GGA GCG ATC CAG TAT GCG CGA AAA TAT GCG TAT TCA GCG GCC TCT GGA GGC CGT CGA AGT GCA ACA CTT AAA GTA ATG GTG	Integrin α ₂ subunit (CD49b, VLA-2, platelet gpIa) I domain	CN I-IV, LN, Echovirus-1 receptor	Thromb, Ather, SIRS, MOF, SS, ID	4
9	D-6	TAC AAC GTC GAC ACA GAA TCT GCA CTT TTA TAT CAG GGC CCG CAT AAT ACA CTG TTT GGC TAC AGT TGG CTC CAC TCC CAT GGA GCT CAT AGA TGG CTA CTG GTA AGA TGG CTA CTG GTA GGA GCG CCA ACA GCA ATG TGG TTA GCA ATG GCA AGC GTT ATT AAT CCT GGG GCC ATC TAT AGA TGC AGA ATA GGA AAA AAC CCA GGG CAG ACG TGT GAA TTG CAA TTG GGT TCA TTC CAC GGT GAG CCC GGC GGT AAG ACT TGT CTA GAG GAA AGA GAT CAC CAA TGG CTT GGG GTG ACC CTC TCG AGA	Integrin α ₄ subunit (CD49b, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	5
11	D-7	CIC ICG AGA CAG GAT TAT GTA AAG AAA TTC GGC GAA CAT TTT GCA AGT TGT CAA GCA GGG ATA TCC TCG TTC TAT ACG AAA GAC TTA ATC GTA ATG GGT GCA CCA GGA TCT TCA TAC TGG ACA GGA AGC TTA TTT GTA TAC ATG ATT ACC ACT AAT AAG TAT AAA	Integrin α ₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	5

SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
13	D-8	CAG GAT TAT GTA AAG AAA TTC GGC GAA CAT TTT GCA AGT TGT CAA GCA GGG ATA TCC TCG TTC TAT ACG AAA GAC TTA ATC GTA ATG GGT GCA CCA GGA TCT TCA TAC TGG ACA GGA AGC TTA TTT GTA TAC ATG ATT ACC ACT AAT AAG TAT AAA	Integrin α₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	5
15	D-9	GGA CAT AGA TGG AAA AAC ATA TTT TAT ATA AAG AAT GAA AAT AAA TTA CCA ACA GGA GGA	Integrin α ₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	6
17	D-10	GGA GGA GCA CCA CAG CAT GAA CAA ATA GGA AAA	Integrin α ₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	6
19	D-11	AGT TAT TGG ACA GGA AGT	Integrin α ₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	6
21	D-12	ATG GGA GCA CCA GGA AGT AGT TAT TGG ACA GGA	Integrin α₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	7
23	D-13	TAC AAT GTA GAT ACA GAA AGT GCA TTA CTC TAT CAA GGT CCA CAC AAC ACA TTG TTT GGG TAT AGT TGG CTT CAT AGT CAT GGA GCA CAC AGA TGG CTG CTA GTA GGC GCA	Integrin α ₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	
	D-14	ATA GTA ACG TGT GGC CAT AGA TGG AAA AAT ATT TTT TAT ATC AAA CAC GAA AAC AAA TTA CCA ACA GGA GGG TGT TAT GGC GTG CCC CCG GAT TTA AGA ACC GAA TTA AGT AAG AGA ATA GCC CCT GGT TAT CAG GAC TAC GTT AAA AAG TTC GGA GAG CAT TTT GCT AGT TGC CAA GCA GGT ATC AGT AGT TTC TAC ACT AAG GAT TTA ATT GTC ATG GGG GCG	Integrin α ₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	8
	D-15	TAC ATG ATT ACC ACT AAC AAG TAT AAA GCG TTT TTA GGG AAG CAA AAT CAG GTG AAG CCA GGA AGT TAT TTA GGG TAT AGT GTA GGT GCC GGC CAT TTC AGA AGT CAA CAC ACG ACA GAA GTT GTC GGC GGT GCA CCA CAA CAT GAG CAG ATA GGA AAA GCT TAC ATC TTT AGT ATA GAT GAA AAA GAA TTA AAT ATA TTA CAC GAG ATG AAG GGA AAA AAA	Integrin α₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	8

SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted	Targeted	Cite
#		<u> </u>		Ligand	Pathology	#
29	D-16	TTA GGA TCA TAT TTC	Integrin α_4 subunit	VCAM-1, FN,	Auto, Ather, SIRS,	8
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GAC GAC ACA GAA GAT TTT GTA GCT GGG GTG CCC AAA GGG AAT TTG ACT TAT GGC TAC GTT ACC ATA CTA AAT GGT TCT GAT ATT CGT AGT TTA TAT AAT TTC AGT GGG GAG CAA ATG GCA AGC TAT TTC GGA TAT GCG GTA GCA GCG GAC GTC AAC GGT GAT GGG CTG GAC GAT TTG CTT GTC GGG GCC CCG TTA CTT ATG GAC CGC ACT CCA GAT GGA AGA CCA CAG GAA GTG GGT CGT GTA TAT GTG TAC TTA CGC GCA CCA GGT TTA CTT ATG GAC CCC ACT CCA GAT GGA AGA CCA CAG GAA GTG GGT CGT GTA TAT GTG TAC TTA CAG CAC CCA GCA GGT ATA GAG CCC CCT GCC GCTTC GCC ACT CGC GCTTC GCC ACT CCA GCA GGT ATA GAG CCC CCG ACT TTG ACC TCC GCC GCTTT GCC ACT CGC CGG TTT GGC AGT TCC GCC CGC AGT TCC ATT GGC AGT TCC ATT GGC AGT TCC ATT GGC AGT TCC ATT GGG GCA CCA TTT GGT GGC ACT TTG GCT ATT GGG GCA CCA TTT GGT GGC	
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GGG CTG GAC GAT TTG CTT GTC GGG GCC CCG TTA CTT ATG GAC CGC ACT CCA GAT GGA AGA CCA CAG GAA GTG GGT CGT GTA TAT GTG TAC TTA CAG CAC CCA GCA GGT ATA GAG CCG ACA CCG ACT TTG ACG CTA ACC GGA CAC GAG TTC GGC CGG TTT GGC AGT TCA TTA ACA CCC CTT GGA GAC TTA GAT CAG GAT GGA TAC AAT GAC GTT GCT ATT GGG GCA CCA TTT GGT GGC	ļ
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CCA CAG GAA GTG GGT CGT GTA TAT GTG TAC TTA CAG CAC CCA GCA GGT ATA GAG CCG ACA CCG ACT TTG ACG CTA ACC GGA CAC GAC TTC GGC CGG TTT GGC AGT TCA TTA ACA CCC CTT GGA GAC TTA GAT CAG GAT GGA TAC AAT GAC GTT GCT ATT GGG GCA CCA TTT GGT GGC	
CGT GTA TAT GTG TAC TTA CAG CAC CCA GCA GGT ATA GAG CCG ACA CCG ACT TTG ACG CTA ACC GGA CAC GAC GAC TTC GGC CGG TTT GGC AGT TCA TTA ACA CCC CTT GGA GAC TTA GAT CAG GAT GGA TAC AAT GAC GTT GCT ATT GGG GCA CCA TTT GGT GGC	
TTA CAG CAC CCA GCA GGT ATA GAG CCG ACA CCG ACT TTG ACG CTA ACC GGA CAC GAC TTC GGC CGG TTT GGC AGT TCA TTA ACA CCC CTT GGA GAC TTA GAT CAG GAT GGA TAC AAT GAC GTT GCT ATT GGG GCA CCA TTT GGT GGC	
GGT ATA GAG CCG ACA CCG ACT TTG ACG CTA ACC GGA CAC GAC TTC GGC CGG TTT GGC AGT TCA TTA ACA CCC CTT GGA GAC TTA GAT CAG GAT GGA TAC AAT GAC GTT GCT ATT GGG GCA CCA TTT GGT GGC	
CCG ACT TTG ACG CTA ACC GGA CAC GAC TTC GGC CGG TTT GGC AGT TCA TTA ACA CCC CTT GGA GAC TTA GAT CAG GAT GGA TAC AAT GAC GTT GCT ATT GGG GCA CCA TTT GGT GGC	
TTC GGC CGG TTT GGC AGT TCA TTA ACA CCC CTT GGA GAC TTA GAT CAG GAT GGA TAC AAT GAC GTT GCT ATT GGG GCA CCA TTT GGT GGC	
AGT TCA TTA ACA CCC CTT GGA GAC TTA GAT CAG GAT GGA TAC AAT GAC GTT GCT ATT GGG GCA CCA TTT GGT GGC	
CTT GGA GAC TTA GAT CAG GAT GGA TAC AAT GAC GTT GCT ATT GGG GCA CCA TTT GGT GGC	
CAG GAT GGA TAC AAT GAC GTT GCT ATT GGG GCA CCA TTT GGT GGC	
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TCA TTG GAA GGT AAC	
CCG GTC GCG TGT ATC AAC CTC TCC TTC TGT	
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CTA CTG ATA CAG AAC	
GGA GCC AGA GAG GAT	}
TGC CGC GAA ATG AAG ATC TAC CTG AGA AAT	[]
GAA TCT GAG TTC CGA]]
GAC AAG TTA TCT CCG	
ATT CAT ATT GCT	ī ļ

SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
33	D-18	AGC TAC CTA GGA TAT	Integrin as subunit	FN, L1, invasin	Thromb, Ather,	10
33	2.0	AGT GTT GCT GTA GGC	(CD49e, VLA-5)		SIRS, ID	ļ
		GAG TTC AGC GGA GAT	(, , , , , , , , , , , , , , , , , ,]
1 1		GAT ACA GAA GAC TTT				1
!!		GTT GCA GGG GTG CCT				1
		AAG GGG AAT CTA ACA TAT GGG TAC GTA ACA				}
1 1		ATC CTC AAC GGA TCG	,		•	1
(GAT ATT CGT AGT TTA				1
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		GAG CAA ATG GCC TCA]		1
		TAT TTT GGA TAC GCC				
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1	1	ATA GTA GGG TCG TTC	ł			1
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	ľ	GTA GTC TAT CGC GGG	·			<u> </u>
35	D-19	GCA CAT GGT TCG AGC	Integrin α_5 subunit	FN, L1, invasin	Thromb, Ather,	11
ļ		ATC TTA GCA TGC GCT	(CD49e, VLA-5)		SIRS, ID	
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		TTA TCG ACC GAC AAC		ľ		
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		AGA TCT GAT TTC AGT				
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1		GGC TTC AGT GCC GAA				-
	1	TTT ACT AAG ACC GGA				
1		AGA GTA GTG CTT GGA	1			1
	1	GGT CCA GGA TCA TAC		Į.		1
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		ATT CTA TCC GCT ACA				1
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i		GAG AGT TAT TAT CCA GAA TAC CTG ATA AAT		Į.		
	İ	TTA GTT CAG GGC CAG			· ·	
	1	TTG CAG ACT AGA CAA		-		
		GCC TCA TCC ATT TAT				L
37	D-20	GAT TTT AGT TGG GCA	Integrin as subunit	FN, L1, invasin	Thromb, Ather,	11
]	1	GCA	(CD49e, VLA-5)	1	SIRS, ID	<u> </u>
L	1	<u> </u>	1 (52 :55, 12.55)			

SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted	Targeted	Cite
#	120 "			Ligand	Pathology	#
39	D-21	GGA GTA GAC GTA GAT CAG GAT GGC GAA ACA GAG TTA ATA GGA GCA CCA TTA TTT TAT GGT GAA CAA AGA GGG	Integrin α _L subunit (CD11a) I domain	ICAM-1, ICAM-2, ICAM-3, LPS,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	12
41	D-22	ATA ACA GAT GGA GAA GCA ACA GAC AGT GGA CAA ATT GAT GCA GCA AAA GAC ATC ATA TAT ATT ATA GGA ATC	Integrin α _L subunit (CD11a) I domain	ICAM-1, ICAM-2, ICAM-3, LPS,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	12
43	D-23	ATA ACA GAT GGA GAA GCA ACA AGT GGA TGT	Integrin α _L subunit (CD11a) I domain	ICAM-1, ICAM-2, ICAM-3, LPS,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	13-
45	D-24	GGA GTA GAC GTA GAT CAA GAT GGA GAA ACA TGT	Integrin α _L subunit (CD11a) I domain	ICAM-1, ICAM-2, ICAM-3, LPS,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	15
47	D-25	TGC CCA AAT AAG GAA AAA GAG TGT	Integrin α _L subunit (CD11a) I domain	ICAM-1, ICAM-2, ICAM-3, LPS,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	16
49	D-26	AAA GAA TIT GTA AGT ACA	Integrin α _m subunit (CD11b) I domain	iC3b, ICAM-1, ICAM-2, ICAM-4, Fb, Factor X, CD23, NIF, heparin, β- glucan, LPS	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	17
51	D-27	CCA ATA ACA CAA TTA TTA GGA AGA ACC CAT ACG GCA ACT GGA ATA AGA AAA	Integrin α_m subunit (CD11b) I domain	iC3b, ICAM-1, ICAM-2, ICAM-4, Fb, Factor X, CD23, NIF, heparin, β- glucan, LPS	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	17
53	D-28	AAA TIT GGA GAC CCA TTA GGA TAT GAA GAT GTA ATA CCA GAG GCA GAT AGA	Integrin α_m subunit (CD11b) I domain	iC3b, ICAM-1, ICAM-2, ICAM-4, Fb, Factor X, CD23, NIF, heparin, β- glucan, LPS	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	17, 18
55	D-29	GGA TGT CCA CAA GAA GAT AGT GAC ATT GCA TTC TTA ATA GAT GGA AGT GGA AGT ATA ATC CCA CAT GAC TTT	Integrin α _m subunit (CD11b) I domain	iC3b, ICAM-1, ICAM-2, ICAM-4, Fb, Factor X, CD23, NIF, heparin, β- glucan, LPS	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	19
57	D-30	TTT AGA AGA ATG AAA GAG TTT GTA AGT ACA GTA ATG GAA CAA TTA AAG AAA AGT AAG ACA TTA TTC AGT	Integrin α _m subunit (CD11b) I domain	iC3b, ICAM-1, ICAM-2, ICAM-4, Fb, Factor X, CD23, NIF, heparin, β- glucan, LPS	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	19

SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
59	D-31	GGA AAT AGT TTT CCA GCA AGT TTA GTA GTA GCA GCA GAA GAG GGA GAG AGA GAA	Integrin α_{IIb} subunit (CD41) heavy chain	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	20
61	D-32	AAC GCA CAA ATC GGA ATT GCA ATG TTA GTA AGT GTA GGA AAT TTA GAG GAA GCA GGA GAA AGT GTA AGT TTT CAA TTA CAG ATA	Integrin α _{IIb} subunit (CD41) heavy chain	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	20
63	D-33	ACA TTA GGA CCA AGT CAA GAA GAG ACA GGA GGA GTA TTT TTA TGT CCA TGG AGA	Integrin α_{Ilb} subunit (CD41) heavy chain	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	20
65	D-34	GCA GAA GGA GGA CAA TGT CCA AGT TTA TTA TTT GAT TTA	Integrin α_{IIb} subunit (CD41) heavy chain	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	20
67	D-35	GCC ATG GTC ACA GTA TTG GCA TTT CTT TGG CTC CCA AGT CTA TAT CAG AGA CCA CTG GAT CAA TTT GTG TTA CAA AGT CAT GCT TGG TTC AAT GTT AGT AGT TTA CCA TAC GCG GTA	Integrin α _{IIb} subunit (CD41) light chain	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	20
69	D-36	GGA GCA CAT TAT ATG AGA GCA TTA AGT AAT GTA GAA	Integrin α_{IIb} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	21
71	D-37	GGA GCA CCA TTA	Integrin α_{IIb} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	22
73	D-38	GGA GAT GGA AGA CAT GAC TTA TTA GTA GGA GCA CCA TTA	Integrin α_{IIb} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	·22
75	D-39	ACA GAT GTA AAT GGA GAC GGA AGA CAT GAT TTA	Integrin α_{llb} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	23
77	D-40	GGA GAT GGA AGA CAT GAC TTA TTA GTA GGA GCA CCA	Integrin α_{lib} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	23
79	D-41	GGA GAC GGA AGA CAT GAT TTA TTA GTA GGA GCA CCA TTA TAT	Integrin α _{11b} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	24

SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted	Targeted	T 6::-
#	"		Derived from	Ligand	Pathology	Cite
81	D-42	GAA TTT GAC GGT GAT	Integrin all subunit	Fb, FN, VN,	Thromb, Ather,	25
1		CTT AAT ACG ACT GAG	(CD41)	TSP, vWF	SIRS, MOF, IR, ID	23
ļ.		TAC GTC GTC GGA GCA	(CD41)	101, 777	SIKS, MOF, IK, ID	1
ł	}	CCA ACT TGG TCG TGG	İ		1	·
ļ	ļ	ACA TTA GGC GCA GTC	•			1
1	}	GAG ATA CTC GAC AGT			j)
1		TAT TAT CAG AGG TTA				1
	1	CAT AGA TTA CGT GCA		j	1	1
}		GAA CAG ATG GCG TCC		i	l	1
j ,		TAC TTT GGT CAC AGC				1
		GTA GCG GTA ACG GAT			[ĺ
		GTG AAC GGA GAC GGC				1
		CGC CAT GAC TTG CTA		1	1	
İ		GTT GGA GCT CCG CTC	•	·	j	
[TAC ATG GAG AGT CGA	İ	(1	
		GCA GAT CGC AAG CTT		1		i
		GCT GAA GTG GGC CGA	1	1	1	1
		GTA TAT CTT TTC CTT	1		·	1
		CAA CCA CGG GGT CCC	1	1		}
		CAC GCC CTA GGC GCT	1	Į		ł
		CCT AGT TTA TTG TTA	1	1	1	Ì
		ACC GGA ACA CAG TTG				Ì
		TAT GGT AGA TTC GGA)	ļ	1	J
		TCT GCA ATA GCG CCA	1	1	1	}
		CTC GGG GAT TTG GAT	1	j .		
		AGA GAT GGC TAT AAC	1			[
		GAT ATA GCT GTG GCC		Ī		
		GCC CCT TAC GGA GGA	İ		-	i i
l l		CCC TCC GGC AGA GGG	1		1	
		CAG GTT CTG GTT TTC			Í	
		CTA GGG CAA AGT GAA	[i .	
		GGG TTA AGG TCA AGA	1		ļ	
		CCG TCT CAA GTC TTA			l	
		GAC TCG CCA TTT CCA	1	1	1	
		ACC GGA AGT GCG TTT		İ	i	
İ		GGG TTC AGT CTC CGT			1	
		GGT GCA GTG GAC ATC		1		
		GAT GAC AAT GGT TAC	}	1		
		CCG GAT CTA ATT GTT		1		
		GGA GCC TAC GGG GCC		1		
		AAT CAA GTA GCA GTA				
		TAT CGG GCG CAG CCC		1		j,
ļ		GTA GTT AAA GCT TCA			[[ļ
1		GTC CAA CTG CTG GTG	}]	
ŀ		CAA GAC AGC CTG AAC]	ĺ
)		CCT GCA	1			l
	D 42		 • • • • • • • • • • • • • • • • • • •	El El Tor	<u> </u>	
83	D-43	GCA GTA ACA GAT GTA AAT GGA GAC GGA AGA	Integrin $\alpha_{\rm lib}$ subunit	Fb, FN, VN,	Thromb, Ather,	26
j			(CD41)	TSP, vWF	SIRS, MOF, IR, ID	(
i		CAT GAT TTA TTA GTA				
		GGA GCA CCA TTA TAT	L	L	L	- 1

85	D-44	TTT TCC TCA GTC GTG ACA CAA GCT GGC GAG	Integrin all subunit	Fb, FN, VN,	Pathology	#
		I እርእ ርእእ GCT GGC GAG	1 michigani Ciji, Subunit	1 1 0, 1 1 1, 7 1 1,	Thromb, Ather,	27
			(CD41)	TSP, vWF	SIRS, MOF, IR, ID	
		TTA GTA TTG GGG GCT			,,,,	1
		CCC GGA GGC TAC TAC		- [
		TTC CTG GGG CTA CTC				
		GCA CAG GCA CCC GTG		İ	.	
i i		GCG GAC ATA TTC TCG TCT TAT AGA CCT GGG	1		1	
l		ATT TTG TTG TGG CAC	\	ĺ		i
		GTC TCC TCT CAG TCT	1	·]		ľ
		TTA AGT TTC GAT AGT	Į.	\ \		
		AGC AAT CCA GAA TAT]			1
		TTT GAC GGA TAC TGG	1	{		
		GGG TAT TCT GTG GCA	}	}		1
		GTC GGT GAG TTC GAT				
		GGT GAT CTG AAT ACT	J.	j		1
		ACA GAA TAT GTG GTA	•			
		GGG GCT CCT ACA TGG	1	1	J	j
		AGT TGG ACT TTA GGC				Į
		GCG GTC GAG ATA TTA	1		1	1
		GAT AGC TAC TAC CAA	l.			
		CGC TTA CAC AGA TTG CGT GCT GAA CAA ATG	1	}	1	}
		GCC TCC TAC TTT GGT				
		CAT TCA GTC GCC GTT	1		1	1
		ACC GAT GTG AAT GGT	ł		1	ł
' l		GAT GGA CGG CAT GAC	1	1 .		ł
		CTC CTA GTT GGA GCT				
		CCA CTT TAC ATG GAG	1	1		ł
		AGC AGA GCG GAC CGA				ŀ
1		AAG TTA GCT GAA GTA	İ	{		ļ
		GGA AGA GTT TAT TTG				1
1		TTC CTA CAA CCG AGG GGC CCG CAT GCG CTT	[İ		1.
Į.		GGC GCA CCT TCC TTA				Ì
l		CTT CTG ACC GGT ACG	[-
}		CAA CTT TAC GGG CGA	· ·			
		TTT GGG TCG GCC ATT		1		
Ì		GCG CCA CTG GGG GAC		}		}
		CTT GAT CGC GAC GGA		ŀ		
		TAT AAC GAC ATC GCA		į		
		GTT GCC GCG CCT TAT				ļ
1		GGA GGC CCA TCG GGT	}			
- 1		CGG GGA CAG GTT CTA GTG TTC CTC GGT CAA				
1		AGT GAA GGC CTC CGT	1			1 1
[AGT AGA CCG AGC CAG				
i		GTA CTG GAC AGT CCG				
		TTT CCC ACG GGC TCG				
		GCT TTT GGT TTT TCA	1			
		TTA AGA GGT GCG GTA				
		GAC ATC GAT GAT AAC		1	1	
,		GGA TAC CCC GAT CTC	1	Ì		
	İ	ATA GTA GGG GCC TAT		1	1	
Ì		GGC GCC AAC CAG GTC GCA GTT TAT AGG GCC				
-		CAG CCA GTA GTG AAA			[
.]		GCA TCA GTC CAA TTA		1		
}		CTA GTT CAG GAC				
87	D-45	GTA GAA AAT GAT TTT AGT TGG	Integrin α_{IIb} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	28
NA	D-46	GAA TAT	Integrin α_{11b} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	28
89	D-47	GGA GAA TTA GTA TTA	Integrin α_{lib} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	28
91	D-48	GAT TTA TAT TAT TTA	All integrin β subunits	FN, Fb, CN I,	All named	29
		ATG GAC TTA AGT TAC AGT ATG AAA		VN	pathologies	

SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
NA	D-49	D\$\$\$\$\$DXSXS\$KDDL; \$, any hydrophobic residue; X, any residue	All integrin β subunits	All named ligands	All named pathologies	29
93	D-50	TAC TGC CGA AAA GAA AAC TCA TCG GAA ATA TGT AGT AAC AAT GGG GAG TGC GTC TGC GGC CAA TGT GTA TGC CGG AAA CGT GAC AAC ACA AAC GAA ATC TAT AGT GGA AAG TTT TGT GAG TGT GAT AGT TTC AAC TGT GAT AGT TGC AGC AAG TGT AGG AGC AAT GGC TTA ATA TGC GGT GGC AAT GGA GTT TGC AAG TGT AGG GTG TGT GAA TGC AAT CCA AAT TAT ACA GGG AGT GCA TGC GAT TGC TCT TTA GAC ACT AGT ACG TGC GAG GCA TCC AAC GGG CAG ATA TGT AAT GGA AGA GGT ATT TGT GAG TGT GGT GTA TGC AAA TGT AGT GGC AAG GGT ATT TGT GAG TGT GGT GTA TGC AAA	Integrin β ₁ subunit (CD29)	FN, LN, CN, VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	30
95	D-51		Integrin β ₁ subunit (CD29)	FN, LN, CN, VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	31

SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite
97	D-52	TTG CGA TTA CGC TCG GGC GAA CCC CAG ACA	Integrin β ₁ subunit	FN, LN, CN, VCAM-1, FN,	Auto, Ather, SIRS,	32
		TTT ACG CTT AAG TTC	(CD29)	MAdCAM-1,	MOF, Trans, SS, ID Crohn's, IBD, IR	ľ
· ·		AAA CGG GCT GAG GAT TAT CCT ATC GAC CTT		TSP, invasin	5, 12B, 1K	
		TAC TAT CTT ATG GAT]
		CTC TCA TAT AGT ATG	,			
ľ		AAA GAT GAT CTG GAG AAT GTT AAG TCC TTA				l
}		GGG ACC GAT TTA ATG				}
1		AAC GAG ATG AGA AGA				ĺ
		ATC ACT TCA GAC TTC AGA ATT GGA TTT GGC				
		TCT TTT GTC GAA AAA				
		ACC GTA ATG CCA TAC				
		ATA AGC ACA ACC CCA GCA AAG CTG AGG AAT		}	1	
		CCG TGT ACA TCG GAG				
		CAA AAC TGC ACT ACT		ĺ		
		CCC TTC AGT TAT AAG)		
		AAT GTT CTC AGT CTG ACG AAC AAA GGG GAA				
		GTA TTT AAC GAG CTA	<u> </u>			
		GTG GGA AAA CAG AGA]		
		ATT AGC GGT AAC CTC GAC TCT CCA GAA GGT				
		GGT TTT GAT GCA ATT		{		
		ATG CAA GTT GCA GTG				
		TGT GGA TCT CTA ATA GGG TGG CGT AAT GTA			[
		ACT AGA CTA TTG GTG]]	j
		TTT TCC ACC GAC GCC				
		GGC TTC CAC TTC GCT GGA GAC GGC AAG CTA				
		GGG GGA ATC GTA ȚTG	•			ļ
	•	CCT AAC GAT GGT CAG TGC CAT TTG GAA AAT		•		l
1		AAT ATG TAT ACG ATG				ł
		TCG CAC TAC TAC GAC				Ì
		TAC CCA TCC ATA GCC CAT TTA GTC CAA AAG				1
		CTG AGC GAA AAC AAT	,			1
		ATT CAA ACA ATA TTT				1
		GCG GTA ACG GAA GAG TTC CAG CCA GTC TAT				-
		AAG GAG CTT AAA AAT				
	•	CTC ATC CCG AAA TCA				1
99	D-53	GCG AAC AAG GGA GAA GTA	Integrin β ₁ subunit	FN, LN, CN,	Auto, Ather, SIRS,	-22
"	در-ر	TTT AAT GAG TTA GTA	(CD29)	VCAM-1, FN,	MOF, Trans, SS, ID	33
		GGA AAA	()	MAdCAM-1,	Crohn's, IBD, IR	
		·		TSP, invasin]
101	D-54	ACA GCA GAA AAA TTA	Integrin β ₁ subunit	FN, LN, CN,	Auto, Ather, SIRS,	34
			(CD29)	VCAM-1, FN, MAdCAM-1,	MOF, Trans, SS, ID	i
				TSP, invasin	Crohn's, IBD, IR	- 1
103	D-55	GAT TAC CCA ATA GAC	Integrin β ₁ subunit	FN, LN, CN,	Auto, Ather, SIRS,	35
		TTA TAC TAT TTA ATG	(CD29)	VCAM-1, FN,	MOF, Trans, SS, ID	
		GAC TTA AGT TAT AGT ATG AAG GAT GAT TTA		MAdCAM-1,	Crohn's, IBD, IR	1
		GAA GTA AAA AGT TTA		TSP, invasin		İ
<u></u>	77.5.5	GGA				
105	D-56	AAT GTA AAG AGT TTA GGA ACA GCA TTA ATG	Integrin β ₁ subunit	FN, LN, CN,	Auto, Ather, SIRS,	36
		AGA GAG ATG GAA AAA	(CD29)	VCAM-1, FN, MAdCAM-1,	MOF, Trans, SS, ID Crohn's, IBD, IR	
		ATA ACA AGT GAT TTT			Civilii S, IBD, IK	-
		AIA NOTA NOT UNI III		TSP, invasin		

SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted	Targeted	Cite
#		•		Ligand	Pathology	#
107	D-57	GGA CAA AAA CAG TTA	Integrin β ₂ subunit	ICAM-1,	Thromb, Auto, SS,	37
		AGT CCG CAG AAG GTC	(CD18)	ICAM-2,	Ather, SIRS, MOF,	"
1		ACT CTA TAC TTG CGT	(0.2.10)	ICAM-3,	Trans, Crohn's,	ļ
1 :		CCC GGG CAA GCA GCC		1		1
		GCG TTC AAC GTA ACG		ICAM-4, LPS,	IBD, bact,	
}		TTT CGT CGC GCA AAA		iC3b, Fb,	hookworm, IR, ID	j
		GGA TAC CCA ATA GAC		Factor X,	1	}
}		CTT TAT TAT TTA ATG		CD23, NIF,	1]
		GAT TTA TCC TAC TCA		heparin, β-		Ì
1		ATG CTC GAT GAT TTA		glucan,	i e	Į
		AGA AAC GTT AAG AAG				
1		TTA GGC GGG GAT CTG			j	Ì
i l		CTC AGA GCT CTC AAT				
)		GAG ATA ACT GAA AGT				
		GGT CGG ATA GGT TTC				
1		GGT TCG TTC GTT GAT				ļ
		AAG ACG GTG CTG CCC				1
1 1	•	TTT GTA AAT ACA CAC				
,		CCA GAC AAA CTG AGG	•			
		AAC CCC TGC CCA AAT				
1 1		AAG GAG AAA GAA TGC		'		
		CAG CCG CCT TTC GCT				
1 (TTT CGC CAT GTC CTA		1		
1		AAA TTA ACA AAT AAT		1		
1 1		AGC AAT CAA TTT CAG	-			
1 1		ACC GAG GTA GGA AAA				
1		CAA CTT ATT AGT GGA		1		
		AAC TTA GAC GCC CCA				
1 1		GAG GGC GGC TTA GAC		1	'	
1		GCA ATG ATG CAA GTA		'		
1 1		GCA GCC TGT CCG GAG		1		
		GAA ATT GGT TGG CGG		ĺ		ĺ
1 1	- 1	AAT GTC ACC AGG TTG		}		
1 1		TTG GTA TTT GCC ACT				.
1 1		GAC GAT GGA TTC CAT			ļ	ļ
		TTT GCT GGA GAT GGC			ļ	
1 1		AAG CTA GGG GCG ATT			j]
1	ļ	CTT ACC CCT AAC GAC				ŀ
1 1		GGG CGA TGT CAC CTC			ļ	}
		GAA GAC AAC CTA TAT	j	,		l
1 1	Ì	AAG AGA AGT AAT GAA	©-	}	j	
		TTC GAT TAT CCA TCT				Į
1	ļ	GTG GGA CAA CTG GCG	j			- 1
1 1		CAT AAG TTG GCT GAG				- (
1	j	AAC AAC ATA CAG CCA	,	Ì		
	ļ	ATC TTT GCA GTT ACA	-	[- 1
]		AGT CGA ATG GTG AAA				
1		ACA TAC GAA AAA CTT		ŀ		ľ
,		ACG GAA ATC ATC CCT	ł	ŀ		
L		AAA AGT GCG				

SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
109	D-58	TAC CCA ATA GAT CTC TAC TAC CTG ATG GAT CTA TCC TAT TCA ATG CTG GAC GAT CTA CGT AAC GTT AAG AAA CTT GGA GGT GAT TTA CTA AGA GCT CTT AAC GAA ATC ACG GAG AGT GGG CGA ATC GGC TTC GGC TCA TTC GTC GAC AAG ACA GTA TTG CCC TTC GTA AAC ACG CAC CCA GAC AAG CTT AGA AAC CCC TGC CCA AAT AAA GAG AAA GAG TGT CAA CCC CGG TTT GCC TTT AGA CAT GTC TTA AAG CTC ACG AAT AAC AGC GAT TTC GGT AAA CCC CGG TTT GCC TTT AGA CAT GTC TTA AAG CTC ACG AAT AAC AGC AAT CAG TTT CAG ACA GAA GTT GGA AAA CAA CTG ATA TCG GGT AAT CTA GAC GCA CCA GAG GGG GGA CTT GAT GCC ATG ATG CAG GTG GCA GCC TGC CCG GAG GAA ATT GGG TGG AGG AAT GTC ACA AGA CTG CTA GTT TTC GCA ACT GAT GTC TCA GAC GAT GGA CCT GCC CG GAG GAA ATT GGG TGG AGT AAA CTG GGC GCA ATT TTG GCT GGA GAT GGT ACA AGA CTG CTA GTT TTC GCA ACT GAT GCT GGC GCA ATT TTG ACT CCT AAC GAT GGA CGG TGT CAT TTG GAA CTG GTC CTT ACT TTT GCT GGA GAT GGA CGG TGT CAT TTG GAA CTG GTC CCT AGT GTA GAT ACA AGA TTC GAC TAT CCT AGT GTA GTT CCT AAC GAT GGA CTT GCT GTG GGC GAC AAG TTA GCA GAA ACA TTT GCG GTT ACA ACA TTT GCG GTT ACA CGG TTA CCT AGT GTA GTT CAC AGT CGC ATG GTG AAA ACA TTT GCG GTT ACC AGT CGC ATG GTG AAA ACA TTT GCG GTT ACC AGT CGC ATG GTG AAA ACA TTT GCG GTT ACC AGT CGC ATG GTG AAA ACA TTT GCG GTT ACC AGT CGC ATG GTG AAA ACA TTT GCG GTT ACC AGT CGC ATG GTG GAA ACTT CCT AGT GTA GTT ACC AGA TTT TCC GAA GAT AGT AGT AAT TTT TTC AGT AGA GAA TTT TTG GAC CAT AAT GCC TTC CCT GAA GAT AGT AGT AAT GCC TTC CTC GAA GAT AGT AGT AAT GCC TTC CTC AAG GTG ACC TTT CAAG GTG ACC TTT CAAG GTG ACC TTT CAAG GTG ACC TAT GAC TCG	Integrin β ₂ subunit (CD18)	Ligand ICAM-1, ICAM-2, ICAM-3, ICAM-4, LPS, iC3b, Fb, Factor X, CD23, NIF, heparin, β- glucan,	Pathology Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	38
111	D-59	AGA AAT GTA AAA AAG	Integrin β ₂ subunit (CD18)	ICAM-1, ICAM-2, ICAM-3,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's,	39
A.			·	ICAM-4, LPS, iC3b, Fb, Factor X, CD23, NIF, heparin, β-glucan,	IBD, bact, hookworm, IR, ID	

SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
113	D-60	CAA CCA CCA TTT GCA	Integrin β ₂ subunit (CD18)	ICAM-1, ICAM-2, ICAM-3, ICAM-4, LPS, iC3b, Fb, Factor X, CD23, NIF, heparin, β- glucan,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	39
115	D-61	TTA ATA AGT GGA AAT TTA	Integrin β ₂ subunit (CD18)	ICAM-1, ICAM-2, ICAM-3, ICAM-4, LPS, iC3b, Fb, Factor X, CD23, NIF, heparin, β- glucan,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	39
117	D-62	GGA CAA TTA GCA CAT	Integrin β ₂ subunit (CD18)	ICAM-1, ICAM-2, ICAM-3, ICAM-4, LPS, iC3b, Fb, Factor X, CD23, NIF, heparin, β- glucan,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	39
119	D-63	GAG CTC TCA GAA GAT TCT AGT AAT GTC GTC CAT TTA ATC AAA AAC GCC TAT AAC AGA GTT TTC TTA GAC CAC AGT GCA CTG CCA GAT ACG TTG AAG GTA ACA TAC GAC AGC TTT TGC TCC AAT GGG GTG ACC CAT AGA AAC CAG CCA AGA GGC GAT TGT GAC GGA GTA CAA ATA AAT GTA CCA ATA ACA TTC CAG GTT AAG GTG ACA GCT ACT GAG TGT ATA CAA GAA CAA AGT TTT GTA ATT AGA GCG CTT GGT	Integrin β ₂ subunit (CD18)	ICAM-1, ICAM-2, ICAM-3, ICAM-4, LPS, IC3b, Fb, Factor X, CD23, NIF, heparin, β- glucan,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	40
121	D-64	GGT TTC ACC GAC ATT GTA ACA GTA CAG GTA TTA CCA CAA TGC GAA TGC AGA TGT AGA GAT CAA AGT AGA GAC AGA AGT TTA TGC CAT GGA AAG GGC TTT TTA GAA TGT GGA ATC TGT AGA TGC GAT ACG GGA TAT ATA GGA AAA AAT TGT GAG TGT CAG ACT CAA GGG	Integrin β₂ subunit (CD18)	ICAM-1, ICAM-2, ICAM-3, ICAM-4, LPS, iC3b, Fb, Factor X, CD23, NIF, heparin, β- glucan,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	40

SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
123	D-65	TGT AAT GCA TTT AAG ATA TTA GTA GTA ATA ACA GAT GGA GAA AAA	Integrin β ₂ subunit (CD18) A domain	ICAM-1, ICAM-2, ICAM-3, ICAM-4, LPS, iC3b, Fb, Factor X, CD23, NIF, heparin, β- glucan,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	41
125	D-66	ACA GGA ATA AGA AAG GTA GTA AGA GAA TTA TTT AAT ATA ACA AAC GGA GCA AGA AAA AAT	Integrin β₂ subunit (CD18) A domain	ICAM-I, ICAM-2, ICAM-3, ICAM-4, LPS, iC3b, Fb, Factor X, CD23, NIF, heparin, β- glucan,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	41
127	D-67	GAT TTA AGT TAT AGT CTC GAC GAT CTG AGA AAT GTA AAG AAA CTT GGA GGA GAC CTA TTA AGA GCA TTG AAC GAA	Integrin β ₂ subunit (CD18)	ICAM-1, ICAM-2, ICAM-3, ICAM-4, LPS, iC3b, Fb, Factor X, CD23, NIF, heparin, β- glucan,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	42, 43
129	D-68	GAC TAT CCC GTA GAC ATA TAC TAC CTT ATG GAT TTA AGT TAC TCC ATG AAG GAC GAT CTC TGG TCA ATT CAG AAC TTG GGA ACA AAA CTA GCA ACA CAA ATG AGA AAG CTG ACA TCG AAT TTA AGA ATA GGA TTT GGA GCA TTC GTA GAT AAA CCA GTA AGC CCT TAT ATG TAT ATC TCT CCA CCG GAA	Integrin β3 subunit (CD 61; platelet glycoprotein gplΠa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	44
131	D-69	GAC GCA CCA GAA GGA GGA TTT GAT GCA ATA ATG CAA GCA ACA GTA	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	45

SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
133	D-70	TTT TCC ATA CAG GTT CGA CAG GTA GAG GAT TAT CCA GTA GAC ATC TAT TAC TTA ATG GAC TTA AGC TAT AGT ATG AAG GAC GAT CTC TGG AGT ATA CAA AAT TTA GGT ACC AAG TTG GCC ACC CAA ATG CGT AAA TTA ACT TCA AAT TTA CGG ATA GGA TTC GGG GCA TTT GTG GAT AAA CCC GTA TCG CCG TAC ATG TAT ATT AGT CCA CCT GAG GCG CTT GAA AAC CCC TGC TAC GAC ATG AAA ACA ACG TGT CTG CCT ATG TTT GGC TAC AAG CAT GTC CTA ACA TTA ACG GAT CAA GTC ACT AGG TTC AAC GAG GAA GTT AAA AAG CAG AGT GTG TCT CGC AAT AGA GAT GTC CCG GAA	Integrin β3 subunit (CD 61; platelet glycoprotein gplIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	46
135	D-71	GGA GTA AGT AGT TGC CAG CAA TGT TTA GCA GTA AGT CCA ATG TGT GCA TGG TGC AGT GAT GAA GCA TTA CCA TTA GGA AGT CCA AGA	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	20
137	D-72	GTA TTA GAA GAC AGA CCA TTA AGT GAT AAA GGA AGT GGA GAT AGT AGT CAA GTA ACA CAG GTA	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	20
139	D-73	AAC ATC AAT TTA ATA TTT GCA GTC ACA GAA AAC GTA GTG AAT CTT TAC CAG AAC TAT AGT GAG CTA ATA CCA GGA ACA ACA GTA GGA GTT CTC AGT ATG GAT AGT AGT AAT GTA CTG CAA TTG ATT GTA GAC GCA TAT GGA AAA ATA AGA AGT	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	20
141	D-74	ATA GGA TIT GGA GCA TTC GTA GAC AAA CCA GTA AGT CCT TAC ATG TAT ATA AGT CCA CCC GAA GCA TTA GAG AAT CCA TGC TAC GAT ATG AAG ACA ACA TGT TTA CCG ATG TTT GGA TAT AAA	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	20
143	D-75	AGT GTA AGT AGA AAT AGA GAT GCA CCA GAA GGA GGA	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpilla)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	47
145	D-76	AGT GTA AGT AGA AAT AGA GAT GCA CCA GAA GGA	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	48

SEQ ID #	ID#	Nucleotide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
147	D-77	AGA AAT AGA GAT GCA	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	48
149	D-78	GAT GCA CCA GAA GGA GGA TTT GAC GCA ATA ATG CAA GCA ACA	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	49
151	D-79	GAT GCA CCA GAA GGA GGA TTT GAC GCA ATA ATG CAA GCA ACA GTA	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	49
153	D-80	GAT GCG CCA GAA GGT GGG TTT GAC GCG ATC ATG CAA GCT ACA GTG TGC GAC GAA AAA ATA GGC TGG AGA AAC GAT GCA AGT CAC CTC CTT GTC TTC ACA ACC GAT GCA AAA ACA CAT ATT GCC CTG GAC GGG AGA TTG GCC GGC ATA GTT CAA CCA AAT GAT GGT CAG TGT CAT GTA GGA TCA GAC AAT CAC TAT TCT GCT AGC ACT ACC ATG GAT TAC CCA TCC TTA GGA TTA ATG ACA GAG AAG CTA TCG CAG AAG	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1, viper and rattlesnake venom components: albolabrin, bitistatin, echistatin, eristostatin	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID, viper and rattlesnake bites	50
155	D-81	ATG GAC TTA AGT TAT AGT ATG AAA GAT GAT TTA TGG AGT ATA	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	51
157	D-82	GGA CCA AAT ATA TGT ACA	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	52
159	D-83	GGA CCA AAT ATA TGT ACA ACA AGA GGA GTAAGT AGT TGC	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIlIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	52
161	D-84	AAA GAT TCT TTA ATA GTA CAG GTA ACA TTT GAC TGT GAC TGT GCA TGT CAG GCA CAA GCA GAA CCC AAC TCG CAT AGA TGC AAC ACT GGA AAT GGC ACA TTC GAA TGC GGA GTA TGC AGA TGC GGA CCG GGT TGG TTA GGG AGT CAG TGT GAA TGC TCA GAG GAA GAT TAT AGA CCT TCC CAA CAA GAT GAG	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, LI	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	53

SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted	Targeted	Cite
#				Ligand	Pathology	#
163	D-85	CCT ACT TGC CCG GAT GCT TGC ACT TTT AAA AAA GAA TGT GTA GAA TGC AAA AAA TTT GAC CGT GAG CCC TAT ATG ACA GAA AAT ACT TGC AAC AGG TAT TGT AGA GAT GAA ATA GAG AGC GTT AAA GAG TTA AAA GAT ACA GGT AAA GAT GCA GTT AAC TGT ACA TAT AAA AAT GGG GAC GAT TGT GTG GTA CGA TTC CAA TAT TAT GAA GAC AGT TCA GGA AAA TCT ATA TTG TAT GTA GTG GAA GAG CCA GAA TGT CCA AAA GGG	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	54
165	D-86	AAA GAT GAC TTA TGG	Integrin β ₃ subunit (CD 61; platelet glycoprotein gplIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	55
167	D-87	AGT GTA AGT AGA AAT AGA GAT GCA CCA GAA GGA GGA TTT	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	24
169	D-88	CAC GTG GGG AGT GAC AAC CAT TAT TCC GCA TCT ACA ACT ATG GAC TAT CCA AGT CTG GGC TTA ATG ACA GAG AAG TTA AGC CAA AAG AAT TTA AAC TTG ATC TTT GCA GTT ACA GAG AAC GTA GTC AAT CTT TAC CAG AAT TAC AGT GAG CTA ATT CCA GGA ACG ACC GTA GGA GTA TTG TCG ATG GAT AGT TCA AAT GTC CTC CAA CTA ATA GTG GAT AGT ACT GGT AAA ATA AGA AGT AAA GTT GAA TTA GAA GTA AGA GAT CTC CCA GAA GAA CTT AGT CTC	Integrin β3 subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	56

SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
171	D-89	GAC GAT AGT AAA AAT TTC AGT ATT CAA GTA CGA CAA GTA GAA GAC TAT CCC GTT GAC ATC TAC TAT CTA ATG GAT TTA AGT TAC AGT ATG AAA GAT GAT TTA TGG AGT ATA CAG AAT TTG GGG ACC AAG CTT GCA ACC CAA ATG AGA AAG CTG ACA TCG AAC TTA AGG ATT GGA TTT GGA GCA TTC GTT GAT AAG CCT GTG TCA CCG TAT ATG TAC ATC TCT CCC CCA GAG GCT TTA GAA AAT CCG TGT TAC GAC ATG AAA ACG ACA TGT TTA CAT ATG TAC ACG TTA CAT GTT TAC GAC ATG AAA ACG ACA TGT TTA CCT ATG TTT GGT TAT AAA CAT GTA TTA ACG CTC ACT GAC CAG GTA ACA CGT TTT AAC GAA GAG GTC AAG AAA CAG AGG GTC CAG GAA CCG GAT TCC CCG GAG GGC GCA GCC CATA ATG CAA GCA ACT GTC TGC GAC GCC ATA ATG CAA GCA ACT GTC TGC GAC	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP, BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	57
173	D-90	TAT ATG TAC ATA AGT CCC CCG GAA GCA TTA GAG AAT CCT TGT TAC GAT ATG AAA ACT ACC TGC TTA CCA ATG TTT GGA TAT AAG CAT GTA TTA ACA TTA ACG GAC CAA GTA ACA AGA	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	
175	D-91	AGA AAT AGA GAT GCA TAT	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	58
177	D-92	GAC GCA CCA GAA GGA GGA TTT GAT GCA ATA ATG CAA GCA ACA GTA TAT	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	58
179	D-93	TGC TAT GAT ATG AAA ACA ACA TGT	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1, Coxsackievirus A9	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	31, 59
181	D-94	AAT TTT AGT ATA CAG GTA AGA CAA GTA GAA GAC TAT CCA GTA GAT ATA TAT TAC TTA ATG	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	60
183	D-95	GAT ATG AAA ACA ACA	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, LI	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	28

SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
185	D-96	ATA AGT CCA CCA GCA	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	61
187	D-97	AAA CAA AGT GTA AGT AGA AAT AGA GAT GCA CCA GAA	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	62
189	D-98	GAT GAC AGT AAA AAT TITT AGT ATC CAG GTA AGA CAG GTA GAA GAT ATA CCA GTC GAC ATA TAT TAC CTC ATG GAC CTG AGT TAC AGT ATG AAG GAT GAT CTC TGG TCA ATT CAA AAT CTA GGG ACT AAG CTT GCG ACG CAA ATG AGA AAA TTG ACA AGC AAT TTA CGA ATT GGA TTT GGA GCA TTC GTC GAT AAG CCT GTT AGT CCT TAC ATG TAC ATC TCA CCC CCT GAA GCC TTA GAG AAC CCC TGC TAT GAC ATG AAA ACC ACA TGT TTA CCG ATG TTT GGT TAT AAA CAT GTG CTC ACG CTT ACG GAC CAA GTG ACT CGG TTC AAT GAG GAA GTA AAA AAG CAG TCT GTC AGT AGG AAC CCT GTA GAC CAG TCT GTC AGT AGG CAG TCT GTC AGT AGG AAC CGT GAT GAC CCG GCA AGT TTG GAC GCG ATA ATG CAA GCC ACA GTA TGT GAC GAG AAA ATA GGC TGG CGC AAC GTA TGT GAC GAG AAA ATA GGC TGG CGC ACA GTA TGT GAC GAG AAA ATA GGC TGG CGC ACC ACT GAT GCA TCC CAT TTA CTG GTG TTC ACC ACT GAT GCA ATG GAT GGT AGA TTG GAC CAC ATC GCA TTG GAT GGT AGA TTG GCT GGA AGA ACA CAC ATC GCA ATG GTT GGC AAA CAC ATC GCA ATG GTT GGC AAC CAC ATG GAC CAA GTT GGC AAA ACA CAC ATC GCA ATG GTT AGG AAC CAC TAT TCG GCA AAT GAT GGC CAA TGC CAC TAT TCG GCA AAT GAT GGC CAA TGC CAC ATG TTA ACC CAC ATG TTA GGT ACC ACG ATG GAC TAC CAC ATG TTA GAC ACC ATG TTA GGT ACT ACC GAA AAC ACC TAT TCG GCA AAC CAC TAT TCG GCA AAC CAC TAT TCG GCA AAC CAC TAT TCG GCA AAC CAC ATC TCC GTT AAC CTA ATC TTC GCT GTA ACA GAA AAA ACA ACTA CTG GAA AAC ACTA TTA CTG GAA ACC ACTA TTA CTG GAA ACC ACTA TTA CTG GAA ACC ACTA TTA CTG GAA ACC ACTA TTA CTG GAA ACC ACTA TTA CTG GAA ACC ACTA ATC TTC GCT GTA ACA GAA AAT GTA ACT GAG AAG AAC CTT AAC CTA ATC TTC GCT GTA ACA GAA AAT GTA GTT TTA CAG CTA ATT GTT GGG GTC TTG TCC ATG GAC TCA AGT AAT GTT TTA CAG CTA ATT GTT GGG GTC TTG TCC ATG GAC TCA AGT AAT GTT TTA CAG CTA ATT GTT GGG GTC TTG TCC ATG GAC TCA AGT AAT GTT TTA CAG CTA ATT GTT GGG GTC TTG TCC ATG GAC TCA AGT AAT GTT TTA CAG CTA AGT AGA GAT AGA GTT AGA GAT TTA GAA GTT AGA GAT TTA GAA GTT AGA GAT TTA GAA GTT AGA GAT TTT CCA GAG GAG CTC TCT CTG TCT	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	63

SEQ ID	ID#	Nucleotide Sequence	Derived from	Townstad	7	
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	D 00	GAT GAT TCT AAG AAT	 	Ligand	Pathology	#
191	D-99	TTT TCC ATC CAG GTT	Integrin β ₃ subunit (CD	Fb, FN, VN,	Thromb, Auto, SS,	63
l i		CGA CAG GTC GAA GAT	61; platelet glycoprotein	TSP, vWF,	Ather, SIRS, MOF,	í
]	}	TAC CCA GTA GAC ATA	gpIIIa)	OP,BSP, LN,	Trans, Crohn's,	
		TAT TAC CTA ATG GAT	1	CN, L1	IBD, bact, SS, IR,	ł
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		AGT ATC CAA AAC CTG			1	Ì
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		ACT GTC TGT GAC GAG				
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1		ATG ACG GAA AAG TTG		*	İ	ł
		TCG CAA	l			

	SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted	Targeted	Cite
-	193	D-100	AAG CAA CTG AAT TTC	7	Ligand	Pathology	. #
	173	D-100	ACG GCC TCT GGA GAG	Integrin β ₇ subunit	VCAM-1 FN,	Auto, SS, MOF,	64
		ĺ	GCA GAG GCC CGC AGA	(LPAM-1)	MAdCAM-1,	Trans, Crohn's,	1
			TGC GCA CGG AGG GAA		E-cadherin	IBD, IR, ID	ì
1		ł	GAG CTC CTA GCT AGG		(cadherin-1)		1
			GGA TGC CCC CTG GAG				
			GAG CTA GAA GAG CCA CGT GGA CAG CAA GAG		•		1
		[GTA CTA CAG GAT CAG		1		1
		l	CCG CTG TCG CAA GGA		•		1
			GCC CGA GGT GAG GGT		Į		
			GCG ACC CAG CTA GCA		İ		
		'	CCA CAA CGC GTA CGC	•			
			GTT ACA TTA CGG CCA				1
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	}		TAT CCG GTG GAT TTA	i]
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1			CTT AGT TAC TCC ATG				}
1			AAG GAT GAT CTA GAA				
1	1		AGG GTA CGC CAA CTG				
			GGT CAT GCC TTA TTG				[{
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	j		GTG AGT ACC GTG CCT				ľ
	į	i	AGC AAA TTG CGT CAC		ļ		1
1	ł	-	CCT TGT CCA ACT AGG				ļ
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}	}	j	AGT CCG TTC TCA TTC				
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	1	. 1	GAA GTC GGC CGG CAA	}	}		
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		- 1	GTG GGC CAG GTG GCG		İ		
	1	}	CAG GCA CTG AGT GCT		j	j	1
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	1	1	GTT TAC CAA GAA CTC TCA AAA TTA ATA CCC	1]	1
	ļ		AAA TCC GCT GTC GGC	}			1
	}]	GAA TTA TCT GAG GAC	1		1	1
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	1		CAA CTC ATC ATG GAC	l		1	1
		1	GCT TAT AAT TCG CTT		J		J
			AGT AGC ACG GTA ACA			1	İ
	-		CTT CCC CCC CCT CTC		1	1	1
	1		CTT CCG CCC GGT GTC	1	Ì	}	ŀ
	- 1		CAT ATT TCT TAT GAG AGT CAA TGT GAA GGG	}			}
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SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted	Targeted	Cita
#				Ligand	Pathology	Cite #
195	D-101	AGT TTT GTT GAT AAA	Integrin β ₇ subunit	VCAM-1 FN,	Auto, SS, MOF,	
		ACA GTC CTG CCG TTC	(LPAM-1)	MAdCAM-1,	Trans Cash-	64
1	1	GTA AGT ACC GTA CCA	(DITEM-1)		Trans, Crohn's,	1
1	! .	AGT AAG TTA CGC CAT		E-cadherin	IBD, IR, ID	
1		CCA TGT CCA ACG AGG	ļ	(cadherin-1)	Į	1
1	l	TTG GAG AGA TGC CAG			· ·	1
1	Ì	TCT CCT TTT TCC TTC CAC	ĺ	1	ŀ	
] ,	ļ	CAT GTC TTA AGC CTA		,	1 `	I .
1		ACT GGT GAC GCT CAA		1	[1
		GCC TTT GAA CGG GAA		İ		
		GTA GGA AGA CAA TCG		[[[[
1		GTG AGT GGG AAC CTT				i i
1		GAT TCA CCC GAA GGA				1
]		GGC TTC GAC GCA ATA		-		
(TTA CAG GCG GCA CTC			į.	1 1
		TGT CAG GAG CAA ATA			<u> </u>	1
1 1		GGA TGG CGA AAT GTT		1		1
		AGT CGT TTA TTA GTG				i
197	D-102	AAA CAA CTC AAT TTC	Integrin β ₇ subunit	VCAM-1 FN,	Auto, SS, MOF,	64
1		ACA GCT AGT GGC GAA	(LPAM-1)	MAdCAM-1.	Trans, Crohn's,	"
1 1		GCA GAG GCT AGG AGA	(E-cadherin	IBD, IR, ID	{ i
[,	TGC GCC AGG CGA GAA		(cadherin-1)	100, 10, 10	[]
1 1		GAA TTA TTG GCA CGC		(Cadilelin-1)	ł	1 1
1		GGG TGT CCC CTG GAG		ļ		1 1
f	•	GAG CTT GAA GAG CCA		}	ł	1 1
1		CGG GGT CAG CAG GAA		ŀ		[
1 1		GTT TTA CAA GAT CAA		ì]]
1 1		CCA TTA AGT CAG GGA				
1 1		GCA CGC GGC GAA GGG		1	}	
		GCG ACA CAA TTA GCG		1		
		CCA CAG CGT GTC AGA		1		J
	į	GTG ACA TTG CGA CCA		1		
{	}	GGA GAG CCT CAA CAG				
	}	TTA CAA GTA CGT TTT				i
1 1		CTT CGG GCC GAG GGT				1
[TAC CCG GTA GAT CTG				1
ļ į	ŀ	TAT TAC CTA ATG GAC				[
<u> </u>	ļ	CTC AGT TAT AGT ATG	•		,	1
1		AAG GAC GAT CTA				

SEQ ID	ID#	Nucleotide Sequence	Derived from	Targeted	Targeted	Cite
#		<u> </u>		Ligand	Pathology	#
199	D-103	GAA AAA CGT GAG GGA	Integrin β ₇ subunit	VCAM-1 FN,	Auto, SS, MOF,	64
1		AAA GCC GAA GAC AGA GGC CAG TGT AAC CAC	(LPAM-1)	MAdCAM-1,	Trans, Crohn's,	1
		GTG AGG ATA AAC CAA		E-cadherin	IBD, IR, ID	}
		ACC GTA ACC TTC TGG		(cadherin-1)	ļ	
		GTC TCG CTT CAG GCA		}	Į.	j
		ACT CAT TGT TTA CCC			ì	1
1		GAA CCA CAT TTG CTA			ł	1
		CGC CTC CGG GCT TTA GGG TTT TCT GAG GAG				1
		CTC ATA GTT GAG CTA		1		ì
		CAC ACG TTA TGT GAC			İ	1
1		TGC AAT TGC TCA GAC	:		1	1
1 1		ACG CAA CCA CAA GCG				1
		CCA CAC TGT TCC GAT				(
}		GGG CAG GGC CAC CTT]
1 1		CAA TGT GGA GTC TGT AGT TGC GCT CCT GGT				i
1 1		AGA TTG GGT AGG CTG		ŀ		
		TGC GAG TGC AGT GTA				
1 1		GCT GAG TTA TCG AGT				ļ
]		CCT GAT CTC GAA AGC				1
		GGA TGT CGC GCG CCG		1		
)		AAT GGG ACT GGA CCT				
) 1		CTG TGT TCC GGA AAA GGG CAT TGC CAG TGT	•			Ì
) !		GGT CGG TGC TCT TGC		}	!	
1		TCG GGT CAG TCA AGT		į		[
1 1	ŀ	GGC CAT TTG TGC GAA				j l
	1	TGT GAC GAC GCC AGC		Ì		
1 1	ľ	TGT GAA CGG CAT GAG				
1 1	1	GGC ATT TTG TGC GGG				
	ļ	GGT TTC GGC AGG TGC CAG TGT GGG GTG TGT	l	i		
]	j	CAC TGT CAT GCA AAC				
1 1	1	CGA ACA GGT CGA GCA		ĺ		}
1	ļ	TGC GAG TGT TCC GGC				
1	į	GAC ATG GAT TCT TGT		[Ì
1 1	ì	ATA AGT CCG GAG GGA]		
1	i	GGT TTA TGC AGT GGT CAT GGA AGA TGC AAG				ľ
] [ľ	TGC AAT CGC TGC CAA)
		TGC TTA GAT GGT TAC				
1	1	TAC GGA GCC CTA TGT				1
}	}	GAT CAG TGC CCA GGC]
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1	. }	GCG TTT AGA ACA GGC				1
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1	i	GCT CAC ACT AAT GTG	·			j
	ì	ACG CTT GCA CTT GCG				
1 1		CCC ATA TTA GAT GAC				1
		GGC TGG TGT AAA GAA AGA ACA TTG GAT AAC		1		
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	}	GCC AGA GGC ACG GTA	({	1	1
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	ļ	CCG CAA GAA AAG GGA		ĺ	1	- 1
	1	GCA GAT CAT ACC CAA			1	j
	}	GCA ATT GTA CTG GGG TGT GTT GGG GGA ATC		•		1
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	Ì	GGG CTC GTA CTT GCG		ļ	ļ	-
	1	TAT CGT TTA TCA GTC		į	1	Į
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SEQ ID #	ID#	Nucleotide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
201	D-104	GAA CAT ATA CCA GCA	Mimics Integrin α _{IIb} β ₃ subunit	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	65
203	D-105	ATA CCA TGT AAT AAC AAA GGA GCA CAT AGT GTA GGA TTA ATG TGG TGG ATG TTA GCA AGA	67 kD LN receptor	LN	Meta	66
205	D-106	AAA GTA ATA TTA GAT AGA GGA GGA AGT GTA TTA GTA ACA TGT	ICAM-1	Fb	Thromb, Ather, SIRS, MOF, IR, ID	67
207	D-107	TGC TGG GAC GAT GGA TGG TTA TGT	Phage display library- mimics RGD binding site in integrins	FN, VN	Thromb, Ather, SIRS, MOF, IR, ID	55
209	D-108	TGC TGG GAT GAC TTA TGG TTA TGT	Phage display library- mimics RGD binding site in integrins	FN, VN	Thromb, Ather, SIRS, MOF, IR, ID	55
211	D-109	TGC TTA TTA AGA ATG AGA AGT ATA TGT	Phage display library	ICAM-1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	68
213	D-110	CCA GAT ACA AGA CCC GCC CCT GGA AGT ACA GCA CCG CCA GCG CAT GGA GTA ACA AGT GCT	MUC-1 protein	ICAM-1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	69
215	D-111	GAG TGG TGT GAA TAT TTA GGA GGA TAT TTA AGA TGC TAC GCA	Phage display library	ICAM-1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	70
217	D-112	GAA TGG CCA GAG TAT TTA	Rhinovirus coat protein 14	ICAM-1	Thromb, Auto, IBD, Ather, SIRS, MOF, Trans, Crohn's, SS, IR, ID	70

Ligand Abbreviations

CN I- Type I collagen

CN II- Type II collagen

CN III- Type III collagen

Up to 19 different collagen types

LN- Laminin

VCAM-1- Vascular cell adhesion molecule-1

FN- Fibronectin

MadCAM-1- Mucosal addressin cell adhesion molecule-1

TSD-Thrombospondin

ICAM-1- Intercellular adhesion molecule-1

ICAM-2- Intercellular adhesion molecule-2

ICAM-3- Intercellular adhesion molecule-3

ICAM-4- Intercellular adhesion molecule-4

LPS- bacterial lipopolysaccharide

iC3b-Complement fragment iC3b

Fb- Fibrinogen

VN- Vitronectin

vWF- von Willebrand factor

Pathology Abbreviations

Thromb-Thrombosis

Ather-Atherosclerosis

SIRS- Systemic inflammatory response syndrome

MOF- Multiple organ failure

Auto- Autoimmune diseases

ID- Inflammatory diseases

Trans- Allograft transplant rejection

Crohn's- Crohn's disease (one type of inflammatory disease)

IBD- Inflammatory bowel disease

NIF- hookworm neutrophils inhibitory factor

Bact- Bacterial infection

SS- Septic shock

IR- Ischemia-reperfusion injury

Meta- Metastasis, cancer

ADDENDUM B

TABLE 2 – PEPTIDE SEQUENCES

TABLE 2 - PEPTIDE SEQUENCES

SEQ ID#	ID#	Peptide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
2	P-1	TYKTKEEMIVATSQTSQY	Integrin α ₂ subunit (CD49b, VLA-2, platelet gpla) I domain	CN I-IV, LN, Echovirus-1 receptor	Thromb, Ather, SIRS, MOF, SS, ID	1
NA	P-2	TYK	Integrin α ₂ subunit (CD49b, VLA-2, platelet gpla) I domain	CN I-IV, LN, Echovirus-1 receptor	Thromb, Ather, SIRS, MOF, SS, ID	2
4	P-3	QTSQY	Integrin α ₂ subunit (CD49b, VLA-2, platelet gpla) I domain	CN I-IV, LN, Echovirus-1 receptor	Thromb, Ather, SIRS, MOF, SS, ID	2
6	P-4	IAVIG	Integrin α ₂ subunit (CD49b, VLA-2, platelet gpIa) I domain	CN I-IV, LN, Echovirus-1 receptor	Thromb, Ather, SIRS, MOF, SS, ID	3
8	P-5	TKEEMIVATSQTSQYGGDL TNTFGAIQYARKYAYSAAS GGRRSATIKVMVVVTDGES HDGSMLKAVIDQCNHDNIL RFGIAVLGYLNRN	Integrin α ₂ subunit (CD49b, VLA-2, platelet gpla) I domain	CN I-IV, LN, Echovirus-1 receptor	Thromb, Ather, SIRS, MOF, SS, ID	4
10	P-6	YNVDTESALLYQGPHNTLF GYSWLHSHGAHRWLLVG APTAMWLAMASVINPGAI YRCRIGKNPGQTCEOLQLG SFHGEPGGKTCLEERDHQ WLGVTLSR	Integrin α_4 subunit (CD49b, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	5
12	P-7	QDYVKKFGEHFASCQAGIS SFYTKDLIVMGAPGSSYWT GSLFVYMITTNKYK	Integrin α₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	5
14	P-8	QDYVKKFGEHFASCQAGIS SFYTKDLIVMGAPGSSYWT GSLFVYMITTNKYK	Integrin α ₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	5
16	P-9	GHRWKNIFYIKNENKLPTG G .	Integrin α₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	6
18	P-10	GGAPQHEQIGK	Integrin α₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	6
20	P-11	SYWTGS	Integrin α₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	6
22	P-12	MGAPGSSYWTG	Integrin α₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	7
24	P-13	YNVDTESALLYQGPHNTLF GYSWLHSHGAHRWLLVG A	Integrin α₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	8
26	P-14	IVTCGHRWKNIFYIKHENK LPTGGCYGVPPDLRTELSK RIAPGYQDYVKKFGEHFAS CQAGISSFYTKDLIVMGA	Integrin α ₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	8

SEQ ID#	ID#	Peptide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite
28	P-15	YMITTNKYKAFLGKQNQV KPGSYLGYSVGAGHFRSQ HTTEVVGGAPQHEQIGKA YIFSIDEKELNILHEMKGKK	Integrin α ₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	8
30	P-16	LGSYFGASVGAVDLHADG FSDLLVGAPMQSTIREEGR VFVYINSGSGAVMNAMET NLVGSDKYAARFGESIVNL GDIDNDGFEDVAIGAPQED DLQGAIYIYNGRADGISSTF SQRIEGLQISKSLSMFGQSIS GQIDADNNGYVDVAVGAF RSDRSDSAVLLRTRPVVIV DASLSHPESVNRTKFDCVE NGWPSVCIDLTLCFSYKGK EVPGYIVLFYNMSLDVNRK AESPPRFYFSSNGTSDVITG SIQVSSREANCRTHQAFMR KDVRDILTPIQIEAAY	Integrin α ₄ subunit (CD49d, VLA-4)	VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	8
32	P-17	SSIYDDSYLGYSVAVGEFS GDDTEDFVAGVPKGNLTY GYVTILNGSDIRSLYNFSGE QMASYFGYAVAATDVNG DGLDDLLVGAPLLMDRTP DGRPQEVGRVYVYLQHPA GIEPTPTLTLTGHDEFGRFG SSLTPLGDLDQDGYNDVAI GAPFGGETQQGVVFVFPGG PGGLGSKPSQVLQPLWAAS HTPDFFGSALRGGRDLDGN GYPDLIVGSFGVDKAVVYR GRPIVSASASLTIFPAMFNP EERSCSLEGNPVACINLSFC LNASGKHVADSIGFTVELQ LDWQKQKGGVRRALFLAS RQATLTQTLLIQNGAREDC REMKIYLRNESEFRDKLSPI HIA	Integrin α ₅ subunit (CD49e, VLA-5)	FN, L1, invasin	Thromb, Ather, SIRS, ID	
34	P-18	SYLGYSVAVGEFSGDDTED FVAGVPKGNLTYGYVTILN GSDIRSLYNFSGEQMASYF GYAVAATDVNGDGLDDLL VGAPLLMDRTPDGRPQEV GRVYVYLQHPAGIEPTPTL TLTGHDEFGRFGSSLTPLG DLDQDGYNDVAIGAPFGG ETQQGVVFVFPGGPGGLGS KPSQVLQPLWAASHTPDFF GSALRGGRDLDGNGYPDLI VGSFGVDKAVVYRG AHGSSILACAPLYSWRTEK	Integrin α ₅ subunit (CD49e, VLA-5) Integrin α ₅ subunit	FN, L1, invasin	Thromb, Ather	10.
30	r-19	EPLSDPVGTCYLSTDNFTRI LEYAPCRSDFSWAAGQGY CQGGFSAEFTKTGRVVLGG PGSYFWQGQILSATQEQIA ESYYPEYLINLVQGQLQTR QASSIY	Integrin α ₅ subunit (CD49e, VLA-5)	riv, Li, invasin	Thromb, Ather, SIRS, ID	11
38	P-20	LACAPL	Integrin α ₅ subunit (CD49e, VLA-5)	FN, L1, invasin	Thromb, Ather, SIRS, ID	11
40	P-21	GVDVDQDGETELIGAPLFY GEQRG	Integrin α _L subunit (CD11a) I domain	ICAM-1, ICAM-2, ICAM-3, LPS,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	12

SEQ ID#	ID#	Peptide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
42	P-22	ITDGEATDSGQIDAAKDIIY IIGI	Integrin α _L subunit (CD11a) I domain	ICAM-1, ICAM-2, ICAM-3, LPS,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	12
44	P-23	PENITDGEATSGC	Integrin α _L subunit (CDI Ia) I domain	ICAM-1, ICAM-2, ICAM-3, LPS,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	13- 14
	P-24	PENGVDVDQDGETC	Integrin α _L subunit (CD11a) I domain	ICAM-1, ICAM-2, ICAM-3, LPS,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	15
48	P-25	CPNKEKEC	Integrin α _L subunit (CD11a) I domain	ICAM-1, ICAM-2, ICAM-3, LPS,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	16
50	P-26	LIDGSG	Integrin α _m subunit (CD11b) I domain	iC3b, ICAM-1, ICAM-2, ICAM-4, Fb, Factor X, CD23, NIF, heparin, β- glucan, LPS	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	17
. 52	P-27	PKEFQNNPNPRSLVKP	Integrin α_m subunit (CD11b) I domain	iC3b, ICAM-1, ICAM-2, ICAM-4, Fb, Factor X, CD23, NIF, heparin, β- glucan, LPS	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	17
54	P-28	ARKNAFKILVVITDGEK	Integrin α_m subunit (CD11b) I domain	iC3b, ICAM-1, ICAM-2, ICAM-4, Fb, Factor X, CD23, NIF, heparin, β- glucan, LPS	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	17, 18
56	P-29	GCPQEDSDIAFLIDGSGSIIP HDF	Integrin α _m subunit (CD11b) I domain	iC3b, ICAM-1, ICAM-2, ICAM-4, Fb, Factor X, CD23, NIF, heparin, β- glucan, LPS	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	19
58	P-30	FRRMKEFVSTVMEQLKKS KTLFS	Integrin α _m subunit (CD11b) I domain	iC3b, ICAM-1, ICAM-2, ICAM-4, Fb, Factor X, CD23, NIF, heparin, β- glucan, LPS	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	19
60	P-31	GNSFPASLVVAAEEGERE	Integrin α_{IIb} subunit (CD41) heavy chain	Fb, FN, VN, TSP, Vwf	Thromb, Ather, SIRS, MOF, IR, ID	20

SEQ ID#	ID#	Peptide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
62	P-32	NAQIGIAMLVSVGNLEEAG ESVSFQLQI	Integrin α_{IIb} subunit (CD41) heavy chain	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	20
64	P-33	TLGPSQEETGGVFLCPWR	Integrin α_{lib} subunit (CD41) heavy chain	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID.	20
66	P-34	AEGGQCPSLLFDL	Integrin α_{IIb} subunit (CD41) heavy chain	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	20
68	P-35	AMVTVLAFLWLPSLYQRP LDQFVLQSHAWFNVSSLPY AV	Integrin α_{IIb} subunit (CD41) light chain	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	20
70	P-36	GAHYMRALSNVE	Integrin α_{11b} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	21
72	P-37	GAPL	Integrin α _{IIb} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	22
74	P-38	GDGRHDLLVGAPL	Integrin α_{llb} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	22
76	P-39	TDVNGDGRHDL	Integrin α _{IIb} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	23
78	P-40	GDGRHDLLVGAP	Integrin α_{IIb} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	23
80	P-41	GDGRHDLLVGAPLY	Integrin all subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	. 24
82	P-42	EFDGDLNTTEYVVGAPTW SWTLGAVEILDSYYQRLHR LRAEQMASYFGHSVAVTD VNGDGRHDLLVGAPLYME SRADRKLAEVGRVYLFLQP RGPHALGAPSLLLTGTQLY GRFGSAIAPLGDLDRDGYN DIAVAAPYGGPSGRGQVLV FLGQSEGLRSRPSQVLDSPF PTGSAFGFSLRGAVDIDDN GYPDLIVGAYGANQVAVY RAQPVVKASVQLLVQDSL NPA	Integrin α _{IIb} subunit (CD41)	Fb, FN, VN, TSP,	Thromb, Ather, SIRS, MOF, IR, ID	25
84	P-43	AVTDVNGDGRHDLLVGAP LY	Integrin α_{IIb} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	26
86	P-44	FSSVVTQAGELVLGAPGGY YFLGLLAQAPVADIFSSYRP GILLWHVSSQSLSFDSSNPE YFDGYWGYSVAVGEFDGD LNTTEYVVGAPTWSWTLG AVEILDSYYQRLHRLRAEQ MASYFGHSVAVTDVNGDG RHDLLVGAPLYMESRADR KLAEVGRVYLFLQPRGPHA LGAPSLLLTGTQLYGRFGS AIAPLGDLDRDGYNDIAVA APYGGPSGRGQVLVFLGQS EGLRSRPSQVLDSPFPTGSA FGFSLRGAVDIDDNGYPDL IVGAYGANQVAVYRAQPV VKASVQLLVQD	Integrin α _{Πь} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	27

SEQ ID#	ID#	Peptide Sequence	Derived from	Targeted Ligand	Targeted	Cite
88	P-45	DKLSPIV	Integrin α_{IIb} subunit (CD41)	Fb, FN, VN, TSP, vWF	Pathology Thromb, Ather, SIRS, MOF, IR, ID	28
NA	P-46	QM	Integrin α_{llb} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	28
90	P-47	VVLH	Integrin α_{lib} subunit (CD41)	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	28
92	P-48	DLYYLMDLSYSMK	All integrin β subunits	FN, Fb, CN I, VN	All named pathologies	29
NA	P-49	D\$\$\$\$DXSXS\$KDDL; \$ = any hydrophobic residue; X = any residue	All integrin β subunits	All named ligands	All named pathologies	29
94	P-50	YCRKENSSEICSNNGECVC GQCVCRKRDNTNEIYSGKF CECDNFNCDRSNGLICGGN GVCKCRVCECNPNYTGSA CDCSLDTSTCEASNGQICN GRGICECGVCKCTD	Integrin β ₁ subunit (CD29)	FN, LN, CN, VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	30
96	P-51	See sequence listing	Integrin β ₁ subunit (CD29)	FN, LN, CN, VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	31
98	P-52	LRLRSGEPQTFTLKFKRAE DYPIDLYYLMDLSYSMKD DLENVKSLGTDLMNEMRR ITSDFRIGFGSFVEKTVMPY ISTTPAKLRNPCTSEQNCTT PFSYKNVLSLTNKGEVFNE LVGKQRISGNLDSPEGGFD AIMQVAVCGSLIGWRNVT RLLVFSTDAGFHFAGDGKL GGIVLPNDGQCHLENNMY TMSHYYDYPSIAHLVQKLS ENNIQTIFAVTEEFQPVYKE LKNLIPKSA	Integrin β ₁ subunit (CD29)	FN, LN, CN, VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	32
100	·P-53	NKGEVFNELVGK	Integrin β ₁ subunit (CD29)	FN, LN, CN, VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	33
102	P-54	TAEKL	Integrin β ₁ subunit (CD29)	FN, LN, CN, VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	34
104	P-55	DYPIDLYYLMDLSYSMKD DLENVKSLG	Integrin β ₁ subunit (CD29)	FN, LN, CN, VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	35
106	P-56	NVKSLGTALMREMEKITSD F	Integrin β ₁ subunit (CD29)	FN, LN, CN, VCAM-1, FN, MAdCAM-1, TSP, invasin	Auto, Ather, SIRS, MOF, Trans, SS, ID Crohn's, IBD, IR	36

SEQ	ID#	Peptide Sequence	Derived from	Targeted Ligand	Targeted	Cite
1D#	P-57	GOKOLSPOKVTLYLRPGQ	Integrin β ₂ subunit (CD18)	ICAM-1, ICAM-2,	Pathology Thromb, Auto,	37
108	r-5/	AAAFNVTFRRAKGYPIDLY YLMDLSYSMLDDLRNVKK	integrin p ₂ subunit (CD18)	ICAM-3, ICAM-4, LPS, iC3b,	SS, Ather, SIRS, MOF, Trans,	3/
		LGGDLLRALNEITESGRIGF GSFVDKTVLPFVNTHPDKL RNPCPNKEKECQPPFAFRH		Fb, Factor X, CD23, NIF, heparin, β-	Crohn's, IBD, bact, hookworm,	
		VLKLTNNSNQFQTEVGKQ LISGNLDAPEGGLDAMMQ		glucan,	IR, ID	
		VAACPEEIGWRNVTRLLVF ATDDGFHFAGDGKLGAILT PNDGRCHLEDNLYKRSNEF				
		DYPSVGQLAHKLAENNIQP IFAVTSRMVKTYEKLTEIIP KSA	·			
110	P-58	YPIDLYYLMDLSYSMLDDL RNVKKLGGDLLRALNEITE SGRIGFGSFVDKTVLPFVNT	Integrin β ₂ subunit (CD18)	ICAM-1, ICAM-2, ICAM-3,	Thromb, Auto, SS, Ather, SIRS,	38
		HPDKLRNPCPNKEKECQPP FAFRHVLKLTNNSNQFQTE		ICAM-4, LPS, iC3b, Fb, Factor X, CD23,	MOF, Trans, Crohn's, IBD,	
		VGKQLISGNLDAPEGGLDA MMQVAACPEEIGWRNVTR LLVFATDDGFHFAGDGKL		NIF, heparin, β- glucan,	bact, hookworm, IR, ID	
		GAILTPNDGRCHLEDNLYK RSNEFDYPSVGQLAHKLAE				
		NNIQPIFAVTSRMVKTYEK LTEIIPKSAVGELSEDSSNV VHLIKNAYNKLSSRVFLDH NALPDTLKVTYDSF				
112	P-59	RNVKK	Integrin β ₂ subunit (CD18)	ICAM-1, ICAM-2, ICAM-3,	Thromb, Auto, SS, Ather, SIRS,	39
				ICAM-4, LPS, iC3b, Fb, Factor X, CD23,	MOF, Trans, Crohn's, IBD,	
				NIF, heparin, β-glucan,	bact, hookworm, IR, ID	
114	P-60	QPPFA .	Integrin β ₂ subunit (CD18)	1CAM-1, ICAM-2, ICAM-3,	Thromb, Auto, SS, Ather, SIRS,	39
	·			ICAM-4, LPS, iC3b, Fb, Factor X, CD23,	MOF, Trans, Crohn's, IBD,	
4			*	NIF, heparin, β-glucan,	bact, hookworm, IR, ID	
116	P-61	LISGNL	Integrin β ₂ subunit (CD18)	ICAM-1, ICAM-2, ICAM-3, ICAM-4, LPS, iC3b,	Thromb, Auto, SS, Ather, SIRS,	39
				Fb, Factor X, CD23,	MOF, Trans, Crohn's, IBD, bact, hookworm,	
110	D 62	GQLAH	Integrin β ₂ subunit (CD18)	glucan, ICAM-1, ICAM-2,	IR, ID Thromb, Auto,	39
118	P-62	· ·	integrin p ₂ subunit (CD18)	ICAM-1, ICAM-2, ICAM-3, ICAM-4, LPS, iC3b,	SS, Ather, SIRS, MOF, Trans,	39
				Fb, Factor X, CD23, NIF, heparin, β-	Crohn's, IBD, bact, hookworm,	
120	P-63	ELSEDSSNVVHLIKNAYNK	Integrin β ₂ subunit (CD18)	glucan, ICAM-1, ICAM-2,	IR, ID Thromb, Auto,	40
120		LSSRVFLDHNALPDTLKVT YDSFCSNGVTHRNQPRGD	mogrin p ₂ submit (CD16)	ICAM-3, ICAM-4, LPS, iC3b,	SS, Ather, SIRS, MOF, Trans,	
		CDGVQINVPITFQVKVTAT ECIQEQSFVIRALG		Fb, Factor X, CD23, NIF, heparin, β-	Crohn's, IBD, bact, hookworm,	
				glucan,	IR, ID	

SEQ ID#	ID#	Peptide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
122	P-64	GFTDIVTVQVLPQCECRCR DQSRDRSLCHGKGFLECGI CRCDTGYIGKNCECQTQG	Integrin β ₂ subunit (CD18)	ICAM-1, ICAM-2, ICAM-3, ICAM-4, LPS, iC3b, Fb, Factor X, CD23, NIF, heparin, β-glucan,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	40
124	P-65	CNAFKILVVITDGEK	Integrin β ₂ subunit (CD18) A domain	ICAM-1, ICAM-2, ICAM-3, ICAM-4, LPS, iC3b, Fb, Factor X, CD23, NIF, heparin, β- glucan,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	41
126	P-66	TGIRKVVRELFNITNGARK N	Integrin β ₂ subunit (CD18) A domain	ICAM-1, ICAM-2, ICAM-3, ICAM-4, LPS, iC3b, Fb, Factor X, CD23, NIF, heparin, β-glucan,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	41
128	P-67	DLSYSLDDLRNVKKLGGD LLRALNE	Integrin β ₂ subunit (CD18)	ICAM-1, ICAM-2, ICAM-3, ICAM-4, LPS, iC3b, Fb, Factor X, CD23, NIF, heparin, β-glucan,	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, hookworm, IR, ID	42, 43
130	P-68	DYPVDIYYLMDLSYSMKD DLWSIQNLGTKLATQMRK LTSNLRIGFGAFVDKPVSPY MYISPPE	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	44
132	P-69	DAPEGGFDAIMQATV	Integrin β ₃ subunit (CD 61; platelet glycoprotein gplIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	45
134	P-70	FSIQVRQVEDYPVDIYYLM DLSYSMKDDLWSIQNLGT KLATQMRKLTSNLRIGFGA FVDKPVSPYMYISPPEALE NPCYDMKTTCLPMFGYKH VLTLTDQVTRFNEEVKKQS VSRNRDAPE	Integrin β3 subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, LI	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	46
136	P-71	GVSSCQQCLAVSPMCAWC SDEALPLGSPR 	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, LI	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	20
138	P-72	VLEDRPLSDKGSGDSSQVT QV	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	20
140	P-73	NINLIFAVTENVVNLYÖNY SELIPGTTVGVLSMDSSNV LQLIVDAYGKIRS	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	20

CEO	TD #	Peptide Sequence	Derived from	Targeted Ligand	Targeted	1 000
SEQ ID#	ID#	Tebude seduence	Derived from	Targeted Liganu	Pathology	Cite #
142	P-74	IGFGAFVDKPVSPYMYISPP EALENPCYDMKTTCLPMF GYK	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	20
144	P-75	SVSRNRDAPEGG	Integrin β ₃ subunit (CD 61; platelet glycoprotein gplIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	47
146	P-76	SVSRNRDAPEG	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	48
148	P-77	RNRDA	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, LI	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	48
150	P-78	DAPEGGFDAIMQAT	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	49
152	P-79	DAPEGGFDAIMQATV	Integrin β_3 subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	49
154	P-80	DAPEGGFDAIMQATVCDE KIGWRNDASHLLVFTTDA KTHIALDGRLAGIVQPNDG QCHVGSDNHYSASTTMDY PSLGLMTEKLSQK	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1, viper and rattlesnake venom components: albolabrin, bitistatin, echistatin, eristostatin	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID, viper and rattlesnake bites	50
156	P-81	MDLSYSMKDDLWSI	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	51
158	P-82	GPNICT .	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	52
160	P-83	GPNICTTRGVSSC	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	52
162	P-84	KDSLIVQVTFDCDCACQAQ AEPNSHRCNNGNGTFECG VCRCGPGWLGSQCECSEE DYRPSQQDECSPRE	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	53

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SEQ ID#	ID#	Peptide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
164	P-85	PTCPDACTFKKECVECKKF DREPYMTENTCNRYCRDEI ESVKELKDTGKDAVNCTY KNEDDCVVRFQYYEDSSG KSILYVVEEPECPKG	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	54
166	P-86	KDDLW	Integrin β_3 subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	55
168	P-87	SVSRNRDAPEGGF	Integrin β_3 subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	. 24
170	P-88	HVGSDNHYSASTTMDYPS LGLMTEKLSQKNINLIFAVT ENVVNLYQNYSELIPGTTV GVLSMDSSNVLQLIVDAYG KIRSKVELEVRDLPEELSL	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	56
172	P-89	DDSKNFSIQVRQVEDYPVD IYYLMDLSYSMKDDLWSIQ NLGTKLATQMRKLTSNLRI GFGAFVDKPVSPYMYISPP EALENPCYDMKTTCLPMF GYKHVLTLTDQVTRFNEE VKKQSVSRNRDAPEGGFD AIMQATVCD	Integrin β_3 subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	
174	P-90	YMYISPPEALENPCYDMKT TCLPMFGYKHVLTLTDQV TR	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	57
176	P-91	RNRDAY	Integrin β ₁ subunit (CD 61; platelet glycoprotein gplIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	58
178	P-92	DAPEGGFDAIMQATVY	Integrin β ₃ subunit (CD 61; platelet glycoprotein gplIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	58
180	P-93	CYDMKTTC	Integrin β ₃ subunit (CD 61; platelet glycoprotein gplIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1, Coxsackievirus A9	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	31, 59
182	P-94	NFSIQVRQVEDYPVDIYYL M	Integrin β ₃ subunit (CD 61; platelet glycoprotein gplIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	60
184	P-95	DMKTT	Integrin β ₃ subunit (CD 61; platelet glycoprotein gplIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, LI	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	28

SEQ ID#	ID#	Peptide Sequence	Derived from	Targeted Ligand	Targeted Pathology	Cite #
186	P-96	ISPPA	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	61
188	P-97	KQSVSRNRDAPE	Integrin β_3 subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	62
190	P-98	DDSKNFSIQVRQVEDYPVD IYYLMDLSYSMKDDLWSIQ NLGTKLATQMRKLTSNLRI GFGAFVDKPVSPYMYISPP EALENPCYDMKTTCLPMF GYKHVLTLTDQVTRFNEE VKKQSVSRNRDAPEGGFD AIMQATVCDEKIGWRNDA SHLLVFTTDAKTHIALDGR LAGIVQPNDGQCHVGSDN HYSASTTIMDYPSLGLMTE KLSQKNINLIFAVTENVVN LYQNYSELIPGTTVGVLSM DSSNVLQLIVDAYGKIRSK VELEVRDLPEELSLSFNAT	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	63
192	P-99	DDSKNFSIQVRQVEDYPVD IYYLMDLSYSMKDDLWSIQ NLGTKLATQMRKLTSNLRI GFGAFVDKPVSPYMYISPP EALENPCYDMKTTCLPMF GYKHVLTLTDQVTRFNEE VKKQSVSRNRDAPEGGFD AIMQATVCDEKIGWRNDA SHLLVFTTDAKTHIALDGR LAGIVQPNDGQCHVGSDN HYSASTTMDYPSLGLMTE KLSQ	Integrin β ₃ subunit (CD 61; platelet glycoprotein gpIIIa)	Fb, FN, VN, TSP, vWF, OP,BSP, LN, CN, L1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	63
194	P-100	KQLNFTASGEAEARRCARR EELLARGCPLEELEEPRGQ QEVLQDQPLSQGARGEGA TQLAPQRVRVTLRPGEPQQ LQVRPLRAEGYPVDLYYL MDLSYSMKDDLERVRQLG HALLVRLQEVTHSVRIGFG SFVDKTVLPFVSTVPSKLR HPCPTRLERCQSPFSFHHVL SLTGDAQAFEREVGRQSVS GNLDSPEGGFDAILQAALC QEQIGWRNVSRLLVFTSDD TFHTAGDGKLGGIFMPSDG HCHLDSNGLYSRSTEFDYP SVGQVAQALSAANIQPIFA VTSAALPVYQELSKLIPKSA VGELSEDSSNVVQLIMDAY NSLSSTVTLEHSSLPPGVHI SYESQCEGP	Integrin β ₇ subunit (LPAM-1)	VCAM-1 FN, MAdCAM-1, E-cadherin (cadherin-1)	Auto, SS, MOF, Trans, Crohn's, IBD, IR, ID	64
196	P-101	SFVDKTVLPFVSTVPSKLR HPCPTRLERCQSPFSFHHVL SLTGDAQAFEREVGRQSVS GNLDSPEGGFDAILQAALC QEQIGWRNVSRLLV	Integrin β ₇ subunit (LPAM-1)	VCAM-1 FN, MAdCAM-1, E-cadherin (cadherin-1)	Auto, SS, MOF, Trans, Crohn's, IBD, IR, ID	64

SEQ	ID#	Peptide Sequence	· Derived from	Targeted Ligand	Targeted	Cite
ID#	<u> </u>	VOLUME 4 000 10 100 100 100 100 100 100 100 10			Pathology	#
198	P-102	KQLNFTASGEAEARRCARR EELLARGCPLEELEEPRGQ QEVLQDQPLSQGARGEGA TQLAPQRVRVTLRPGEPQQ LQVRFLRAEGYPVDLYYL MDLSYSMKDDL	Integrin β ₇ subunit (LPAM-1)	VCAM-1 FN, MAdCAM-1, E-cadherin (cadherin-1)	Auto, SS, MOF, Trans, Crohn's, IBD, IR, ID	64
200	P-103	EKREGKAEDRGQCNHVRI NQTVTFWVSLQATHCLPEP HLLRLRALGFSEELIVELHT LCDCNCSDTQPQAPHCSDG QGHLQCGVCSCAPGRLGR LCECSVAELSSPDLESGCR APNGTGPLCSGKGHCQCG RCSCSGQSSGHLCECDDAS CERHEGILCGGFGRCQCGV CHCHANRTGRACECSGDM DSCISPEGGLCSGHGRCKC NRCQCLDGYYGALCDQCP GCKTPCERHRDCAECGAFR TGPLATNCSTACAHTNVTL ALAPILDDGWCKERTLDN QLFFFLVEDDARGTVVLRV RPQEKGADHTQAIVLGCV GGIVAVGLGLVLAYRLSVE IYD	Integrin β ₇ subunit (LPAM-1)	VCAM-1 FN, MAdCAM-1, E-cadherin (cadherin-1)	Auto, SS, MOF, Trans, Crohn's, IBD, IR, ID	
202	P-104.	ЕНІРА	Mimics Integrin α _{IIb} β ₃ subunit	Fb, FN, VN, TSP, vWF	Thromb, Ather, SIRS, MOF, IR, ID	65
204	P-105	IPCNNKGAHSVGLMWWM LAR	67 kD LN receptor	LN	Meta	66
206	P-106	KVILDRGGSVLVTC	ICAM-1	Fb	Thromb, Ather, SIRS, MOF, IR, ID	67
208	P-107	CWDDGWLC	Phage display library- mimics RGD binding site in integrins	FN, VN	Thromb, Ather, SIRS, MOF, IR, ID	55
210	P-108	CWDDLWLC	Phage display library- mimics RGD binding site in integrins	FN, VN	Thromb, Ather, SIRS, MOF, IR, ID	55
. 212	P-109	CLLRMRSIC	Phage display library	ICAM-1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	68
214 .	P-110	PDTRPAPGSTAPPAHGVTS A	MUC-1 protein	ICAM-1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	69
216	P-111	EWCEYLGGYLRCYA	Phage display library	ICAM-1	Thromb, Auto, SS, Ather, SIRS, MOF, Trans, Crohn's, IBD, bact, SS, IR, ID	70
218	P-112	EWPEYL	Rhinovirus coat protein 14	ICAM-1	Thromb, Auto, IBD, Ather, SIRS, MOF, Trans, Crohn's, SS, IR, ID	70

<u>Ligand Abbreviations</u> CN I- Type I collagen <u>Pathology Abbreviations</u> Thromb- Thrombosis

CN II- Type: II collagen CN III- Type III collagen Up to 19 different collagen types LN- Laminin VCAM-1- Vascular cell adhesion molecule-1 FN- Fibronectin MadCAM-1- Mucosal addressin cell adhesion molecule-1 TSP- Thrombospondin ICAM-1- Intercellular adhesion molecule-1 ICAM-2- Intercellular adhesion molecule-2 ICAM-3- Intercellular adhesion molecule-3 ICAM-4- Intercellular adhesion molecule-4 LPS- bacterial lipopolysaccharide iC3b- Complement fragment iC3b Fb-Fibrinogen VN- Vitronectin vWF- von Willebrand factor

Ather- Atherosclerosis
SIRS- Systemic inflammatory response syndrome
MOF- Multiple organ failure
Auto- Autoimmune diseases
ID- Inflammatory diseases
Trans- Allograft transplant rejection
Crohn's- Crohn's disease (one type of inflammatory disease)
IBD- Inflammatory bowel disease
NIF- hookworm neutrophils inhibitory factor
Bact- Bacterial infection
SS- Septic shock
IR- Ischemia-reperfusion injury
Meta- Metastasis, cancer

We claim:

- 1. A therapeutic bioconjugate comprising:
 - a. a hydrophilic polymer; and
 - b. one or more peptides capable of binding specifically to a ligand expressed on a cell surface.
- 2. The bioconjugate of Claim 1 for blocking interactions between cells in a living tissue wherein said ligand is expressed on the surface of at least one of said cells.
- 3. The bioconjugate of Claim 1 for blocking interaction between a cell and an extracellular matrix wherein said ligand is capable of binding to a component of said matrix.
- 4. The bioconjugate of Claim 1 for blocking pathological reactions triggered by cellular interactions in a living tissue.
- 5. The bioconjugate of Claim 1 wherein said peptide comprises the amino acid sequence of the binding portion of an integrin for said ligand.
- 6. The bioconjugate of Claim 5 for blocking cell signaling receptors implicated in the regulation of cellular adhesion, migration, tumor metastasis, proliferation, angiogenesis, bone resorption, apoptosis, or gene expression.
- 7. The bioconjugate of Claim 5 wherein said binding portion is from an integrin α subunit or an integrin β subunit.
- 8. The bioconjugate of Claim 7 comprising one or more peptides selected from the group consisting of SEQ ID NOS 1-202.

- 9. The bioconjugate of Claim 7 wherein said binding portion is a portion of the integrin α_2 subunit (CD49b, VLA-2, platelet gpla) I domain, integrin α_4 (CD49b, VLA-4), integrin α_5 (CD49e, VLA-5) integrin α_L (CD11a) I domain, integrin α_M subunit (CD11b) I domain, integrin α_{11b} I domain, integrin α_{11b} (CD41) heavy chain, integrin α_{11b} (CD41) light chain, integrin β_1 (CD29) subunit, the integrin β_2 (CD18) subunit, integrin β_3 (CD61) subunit, or integrin β_7 (LPAM-1) subunit.
- 10. The bioconjugate of Claim 9 wherein said peptide comprises the binding portion of the integrin α_2 subunit (CD49b, VLA-2, platelet gpla) I domain and binds specifically to ligands CN I, CN II, CN IV, LN or the echovirus-1 receptor.
- 11. The bioconjugate of Claim 9 wherein said peptide comprises a portion of the integrin α_4 (CD49b, VLA-4) subunit that binds specifically to the ligands VCAM-1, FN, MAdCAM-1, TSP or invasin.
- 12. The bioconjugate of Claim 9 wherein said peptide comprises a portion of the integrin α_5 (CD49e, VLA-5) that binds specifically to ligands FN, L1 or invasin.
- 13. The bioconjugate of Claim 9 wherein said peptide comprises a portion of the integrin α_1 (CD11a) I domain that binds specifically to the ligands ICAM-1, ICAM-2, ICAM-3 or LPS.
- 14. The bioconjugate of Claim 9 wherein said peptide comprises a portion of the integrin α_M subunit (CD11b) I domain that binds specifically to the ligands iC3b, ICAM-1, ICAM-2, ICAM-4, Fb, Factor X, CD23, NIF, heparin, beta glucan, or LPS.
- 15. The bioconjugate of Claim 9 wherein said peptide comprises a portion of the integrin α_{I1b} (CD41) heavy chain that binds specifically to the ligands Fb, FN, VN, TSP or vWF.
- 16. The bioconjugate of Claim 9 wherein said peptide comprises a portion of the integrin α_{11b} (CD41) light chain that binds specifically to the ligands Fb, FN, VN, TSP and vWF.

- 17. The bioconjugate of Claim 9 wherein said peptide comprises a portion of the integrin β_1 (CD29) subunit, and binds specifically to the ligands FN,LN,CN,VCAM-1, FN, MAdCAM-1, TSP or invasin.
- 18. The bioconjugate of Claim 9 wherein said peptide comprises a portion of the integrin β_2 (CD18) subunit that binds specifically to the ligands ICAM-1, ICAM-2, ICAM-3, ICAM-4, LPS, iC3b, Fb, Factor X, CD23, NIF, heparin, or betaglucan.
- 19. The bioconjugate of Claim 9 wherein said peptide comprises a portion of the integrin β_3 (CD61) subunit that binds specifically to ligands fibrinogen, fibronectin, vitronectin, thrombospondin, von Willebrand factor, osteopontin, bone sialoprotein, laminins, collagens, or neural cell adhesion molecule L1.
- 20. The bioconjugate of Claim 9 wherein said peptide comprises a portion of the integrin β_7 (LPAM-1) subunit that binds specifically to the ligands VCAM-1, fibronectin, MAdCAM-1, or E-cadherin (cadherin-1).
- 21. The nucleic acids having the sequence coding for peptides of the bioconjugate of Claim8.
- 22. The nucleic acids of Claim 21 selected from the group consisting of SEQ ID NOS 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 86, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 186, 185, 187, 189, 191, 193, 195, 1197, 199 and 201.
- 23. The peptide for preparation of the bioconjugate of Claim 1, said peptide having a sequence selected from the group consisting of SEQ ID NOS 1-112, wherein each sequence comprises additionally an N-terminal and/or a C-terminal cysteine residue.

- 24. The nucleic acids having the sequence coding for a peptide of Claim 23.
- 25. The bioconjugate of Claim 1 wherein said polymer is a polysaccharide or an oligosaccharide.
- 26. The bioconjugate of Claim 1 wherein said polymer is a derivative of a polysaccharide or an oligosaccharide wherein said derivative polymer additionally comprises additional groups capable of reacting chemically with a peptide to form said bioconjugate.
- 27. The bioconjugate of Claim 1 having the formula XY_b wherein X is a low cell-adhesive, hydrophilic polymer, Y is a peptide comprising a portion of the binding site of an integrin for a ligand expressed on a cell surface, and b is greater than 0.
- 28. The bioconjugate of Claim 27 wherein X comprises a polysaccharide or an oligosaccharide.
- 29. The bioconjugate of Claim 27 wherein X comprises a derivative of a polysaccharide or of an oligosaccharide wherein said derivative saccharide comprises reactive groups whereby said derivative saccharide reacts with said peptide to form said bioconjugate.
- 30. The bioconjugate of Claim 29 wherein said reactive group comprises a hydroxyl group.
- 31. The bioconjugate of Claim 25 wherein said polysaccharide or oligosaccharide is selected from the group consisting of agarose, dextran, heparin, chondroitin sulfate, hydroxyethyl starch, and hyaluronic acid.
- 32. The bioconjugate of Claim 1 wherein said polymer comprises a dextran and said peptide comprises the binding portion of an integrin for its ligand.

- 33. The bioconjugate of Claim 1 wherein said polymer is polyvalent and is selected from the group consisting of poly(ethylene glycol), poly(ethylene oxide), poly(vinyl alcohol), poly(acrylic acid), poly(ethylene-co-vinyl alcohol), poly(vinyl pyrrolidone), poly(ethyloxazoline), and poly(ethylene oxide)-co-poly(propylene oxide) block copolymers.
- 34. The bioconjugate of Claim 1 wherein said polymer comprises copolymers, block copolymers, graft copolymers, alternating copolymers, or random copolymers.
- 35. The bioconjugate of Claim 1 wherein said polymer is essentially inert.
- 36. The bioconjugate of Claim 1 wherein said polymer is degradable by hydrolytic or enzymatic means.
- 37. The bioconjugate of Claim 36 wherein said degradable polymer comprises one or more blocks selected from the group consisting of lactic acid, glycolic acid, ε-caprolactone, lactic-coglycolic acid oligomers, trimethylene carbonate, anhydrides, and amino acids.
- 38. The bioconjugate of Claim 1 wherein said polymer is a serum protein.
- 39. The bioconjugate of Claim 38 wherein said serum protein is an albumin.
- 40. The bioconjugate of Claim 1 in a pharmaceutically acceptable carrier.
- 41. The bioconjugate of Claim 1 immobilized on a solid substrate.
- 42. The bioconjugate of Claim 41 wherein said substrate is an implantable medical device.
- 43. The bioconjugate of Claim 42 wherein said medical device is a drug delivery device.
- 44. The bioconjugate of Claim 41 wherein said substrate is a component of an *in vitro* diagnostic device.

- 45. The kit comprising one or more bioconjugates of Claim 1 and reagents and apparatus suitable for administering said bioconjugate to an individual.
- 46. The kit of Claim 45 wherein said bioconjugate is in a pharmaceutically acceptable carrier.
- 47. The biointerface formed on a mammalian tissue, wherein said biointerface comprises a plurality of bioconjugates of Claim 1 bound to a plurality of ligands on said tissue.
- 48. A method of preparing a bioconjugate comprising the steps of:
 - a. providing a hydrophilic polymer having one or more reactive groups;
 - b. providing a bioselective peptide comprising a chemical group capable of reacting with said reactive groups; and
 - c. contacting said polymer and said peptide under conditions whereby said reactive and chemical groups react to form said bioconjugate.
- 49. The method of Claim 48 wherein the reactive groups of said polymer are hydroxyl groups and the chemical group of said peptide is a sulfhydryl group.
- 50. The method of Claim 48 wherein said polymer is a polysaccharide.
- 51. The method of Claim 50 wherein said polysaccharide is activated dextran.
- 52. The method of Claim 50 wherein said polysaccharide is hydroxyl starch.
- 53. The method of Claim 50 wherein said peptide is selected from the group consisting of SEQ ID NOS 7-14, 25-32, 35-38, 43-48, 55-56, 65, 66, 93, 94, 97, 98, 107-110, 119-124, 133-136, 141, 142, 153, 154, 157-164, 171-174, 179-200, 203-212, 215 and 216, said peptide comprising a cysteine residue.

- 54. The method of Claim 50 wherein said peptide is selected from the group consisting of SEQ ID NOS 1-218, said peptide comprising in addition an N-terminal or a C-terminal cysteine residue.
- 55. A method of preparing a bioconjugate comprising the steps of:
 - a. providing a peptide selected from the group consisting of SEQ ID NOS 1-218;
 - b. modifying said peptide by addition of an N-terminal or C-terminal cysteine residue;
 - c. providing an amount of activated dextran; and
 - d. contacting said activated dextran and said modified peptide under conditions, whereby said dextran and said modified peptide react to form said bioconjugate.
- 56. A method for preventing adhesion of a mobile cell to a cell immobilized on a substrate comprising the step of applying a bioconjugate specific for said immobilized cell under such conditions that said bioconjugate forms a cell adhesion barrier on said immobilized cell.
- 57. A method of blocking pathological reactions triggered by cellular interactions in a living tissue, said method comprising the step of administering to the living tissue a bioconjugate selective for a target tissue whereby the bioconjugate forms a cell adhesion barrier at a targeted tissue site.
- 58. The method of Claim 57, wherein said bioconjugate comprises the binding portion of an integrin for a ligand expressed in said target tissue.
- 59. The method of Claim 58 wherein said bioconjugate is administered intravascularly, orally, intramuscularly, intraperitoneally, subcutaneously, cerebrospinally, endovascularly, rectally or topically.
- 60. The method of Claim 59 wherein said bioconjugate is administered intravascularly in a biologically compatible solution at a concentration of between about 1 μ g/L and 100 g/L.

- 61. The method of Claim 58 wherein said bioconjugate is administered to an individual in a pharmaceutically acceptable composition.
- 62. The method of Claim 58 wherein the amount of administered bioconjugate is between about 1-1000 mg/kg body weight.
- 63. The method of Claim 57 for preventing and treating thrombosis, wherein an anticoagulating amount of a bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands expressed on inflamed endovascular cells is administered to tissue containing said inflamed endovascular cells.
- 64. The method of Claim 63 wherein said integrin ligands are CN I-IV, LN, or the Echovirus-1 receptor.
- 65. The method of Claim 63 wherein said peptide is selected from the group consisting of P-2, P-49, and SEQ ID NOS 1, 2, 3-8, 91-106, 129-192, 203 and 204.
- 66. The method of Claim 57 for preventing and treating atherosclerosis, wherein an antiatherosclerotic effective amount of said bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands expressed on or around atherosclerotic cells is administered to tissue containing said atherosclerotic cells.
- 67. The method of Claim 66 wherein said integrin ligands are VCAM-1, FN, MAdCAM-1, TSP, invasin or a combination thereof.
- 68. The method of Claim 66 wherein said peptide is selected from the group consisting of P-49 and SEQ ID NOS 9-38, 59-106, 129-202 and 207-210.
- 69. The method of Claim 57 for preventing and treating systemic inflammatory response syndrome wherein an effective amount of said bioconjugate comprising one or more peptides

capable of binding selectively to integrin ligands expressed on cells in inflamed tissue is administered to said tissue.

- 70. The method of Claim 69 wherein said integrin ligands are FN, L1 or invasin.
- 71. The method of Claim 69 wherein said bioconjugate comprises one or more peptides selected from the group consisting of P-49 and SEQ ID NOS 9-38, 59-106, 129-202 and 207-210.
- 72. The method of Claim 58 for preventing and treating multiple organ failure wherein an failure effective amount of said bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands expressed on cells in affected tissue is administered to said tissue.
- 73. The method of Claim 72 wherein said integrin ligands are ICAM-1, ICAM-2, ICAM-3, LPS or a combination thereof.
- 74. The method of Claim 72 wherein said bioconjugate comprises one or more peptides selected from the group consisting of P-49 and SEQ ID NOS 39-58, 107-128 and 211-218.
- 75. The method of Claim 57 for preventing and treating autoimmune disease wherein an effective amount of a bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands expressed on cells implicated in the autoimmune disease is administered to tissue containing said cells.
- 76. The method of Claim 75 wherein said integrin ligand is VCAM-1, FN, MAdCAM-1, TSP, invasin, ICAM-1, ICAM-2, ICAM-3, LPS, iC3b, ICAM-1, ICAM-2, ICAM-4, Fb, Factor X, CD23, NIF, heparin, β-glucan, LPS, FN, Fb, CN I, VN, FN, LN, CN, Fb, Factor X, CD23, NIF, heparin, β-glucan or a combination thereof.

- 77. The method of Claim 75 wherein said bioconjugate comprises one or more peptides selected from the group consisting of P-2, P-49 and SEQ ID NOS 1-218.
- 78. The method of Claim 57 for preventing and treating inflammatory diseases wherein an effective amount of a bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands expressed on cells of inflamed tissue is administered to a tissue containing said inflamed cells.
- 79. The method of Claim 78 wherein said integrin ligand is CN I-IV, LN, Echovirus-1 receptor, VCAM-1, FN, MAdCAM-1, TSP, Invasin, L1, LPS, ICAM-1-4, iC3b, Fb, Factor X, CD23, NIF, heparin, β-glucan, VN, vWF or a combination thereof.
- 80. The method of Claim 78 wherein said bioconjugate comprises one or more peptides selected from the group consisting of P-2, P-49, and SEQ ID NOS 1-202 and 205-219.
- 81. The method of Claim 58 for preventing and treating allograft transplant rejection wherein an anti-rejection amount of a bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands expressed on T cells implicated in allograft transplant rejection is administered to an individual having transplanted tissue.
- 82. The method of Claim 81 wherein said integrin ligand is VCAM-1, FN, MAdCAM-1, TSP, invasin, ICAM-1-4, LPS, iC3b, Fb, Factor X, CD23, NIF, heparin, β-glucan, LN, CN, vWF, OP, BSP, L1 and E-cadherin.
- 83. The method of Claim 81 wherein said bioconjugate comprises one or more peptides selected from the group consisting of P-49 and SEQ ID NOS 9-30, 39-58, 91-200 and 211-218.
- 84. The method of Claim 81 further comprising concurrent administration of an immunosuppressant.
- 85. The method of Claim 84 wherein said immunosuppressant is cyclosporine.

- 86. The method of Claim 58 for preventing and treating Crohn's disease wherein an effective amount of said bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands expressed on inflamed cells in gut tissue is administered to said gut tissue.
- 87. The method of Claim 86 wherein said integrin ligand is VCAM-1, FN, MAdCAM-1, TSP, invasin, ICAM-1-4, iC3b, Fb, Factor X, CD23, NIF, heparin, β-glucan, CN I, VN, LN, OP, BSP, L1, vWF and E-cadherin.
- 88. The method of Claim 86 wherein said bioconjugate comprises one or more peptides selected from the group consisting of P-49 and SEQ ID NOS 9-30, 30-58, 93-200 and 211-218.
- 89. The method of Claim 58 for preventing and treating inflammatory bowel disease wherein an effective amount of a bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands expressed on inflamed cells in gut tissue is administered to said gut tissue.
- 90. The method of Claim 89 wherein said bioconjugate comprises one or more peptides selected from the group consisting of P-49 and SEQ ID NOS 9-30, 39-58, 91-200 and 21-218.
- 91. The method of Claim 58 for preventing and treating sequelae of a bacterial infection wherein an effective amount of said bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands expressed on secretory membranes is administered to said secretory membranes.
- 92. The method of Claim 91 wherein said bioconjugate comprises one or more peptides selected from the group consisting of P-49 and SEQ ID NOS 39-58, 107-192 and 211-216.
- 93. The method of Claim 58 for preventing and treating sepsis or septic shock, comprising administering an effective amount of a bioconjugate comprising one or more peptides capable of

binding selectively to integrin ligands such as LFA-1, ICAM-1, VCAM-1 and a combination thereof.

- 94. The method of Claim 93 wherein said bioconjugate comprises one or more peptides selected from the group consisting of P2, P-49 and SEQ ID NOS 1-30, 39-58, 91-200 and 211-18.
- 95. The method of Claim 57 for preventing and treating ischemia-reperfusion injury, comprising administering an effective amount of a bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands intravenously.
- 96. The method of Claim 95 wherein said bioconjugate comprises one or more peptides selected from the group consisting of P-49 and SEQ ID NOS 9-30 and 39-218.
- 97. The method of Claim 57 for preventing and treating cancer metastasis, comprising administering wherein an anti-metastasis effective amount of said bioconjugate comprising one or more peptides capable of binding selectively to integrin ligands systemically to an individual or locally to tissue containing or suspected of containing said cancer.
- 98. The method of Claim 97, wherein said bioconjugate comprises one or more peptides selected from the group consisting of P-49 and SEQ ID NOS 91, 92, 203 and 204.
- 99. The method of Claim 57 for treating conditions caused by viper and rattlesnake bites wherein an anti-venom effective amount of said bioconjugate comprising one or more peptides capable of binding selectively to at least one integrin ligand on a bitten tissue site is administered.
- 100. The method of Claim 110 wherein said bioconjugate comprises a peptide having SEQ ID NOS 153 and 154.

101. Therapeutic replacement fluids comprising a bioconjugate of Claim 1 and a pharmaceutically acceptable diluent.

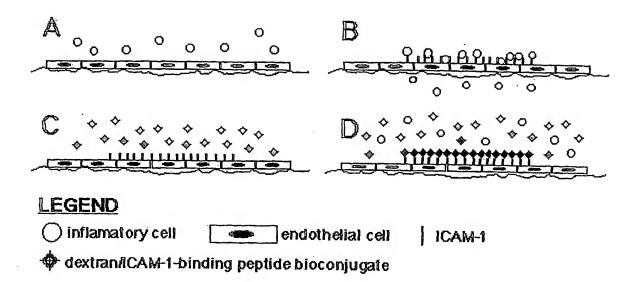


FIGURE 1

FIGURE 2

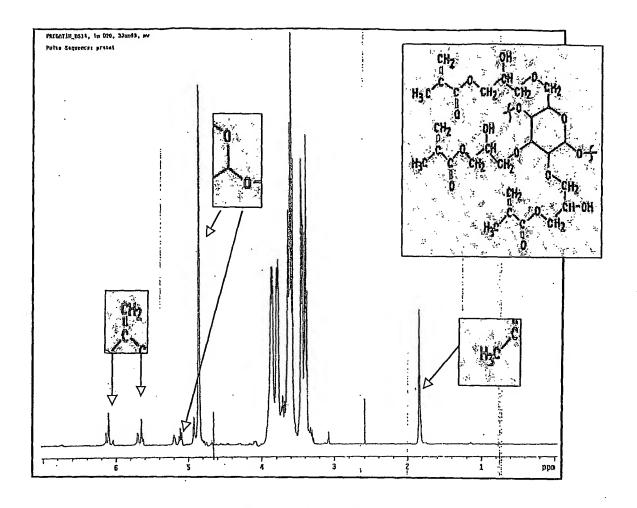


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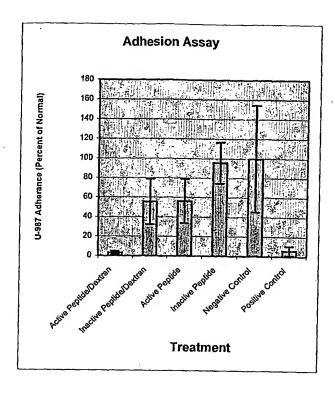


Fig. 2. Monocyte adhesion to bovine endothelial cells. All but the positive control were activated with TNF- α to induce ICAM expression. SM1 is the CD11b/CD18 agonist and SM2 is the scrambled, inactive peptide.

FIGURE 4

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aag act tgt cta gag gaa aga gat cac caa tgg ctt ggg gtg acc ctc 2

Lys Thr Cys Leu Glu Glu Arg Asp His Gln Trp Leu Gly Val Thr Leu

85 90 95

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Ser Arg

Page 6

130588.00025.ST25.txt

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Leu Leu Val Gly Ala Pro Thr Ala Met Trp Leu Ala Met Ala Ser Val 35 40 45

Ile Asn Pro Gly Ala Ile Tyr Arg Cys Arg Ile Gly Lys Asn Pro Gly 50 55 60

Gin Thr Cys Glu Leu Gln Leu Gly Ser Phe His Gly Glu Pro Gly Gly 65 70 75 80

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1 5 10 15

ggg ata tcc tcg ttc tat acg aaa gac tta atc gta atg ggt gca cca 96 Gly Ile Ser Ser Phe Tyr Thr Lys Asp Leu Ile Val Met Gly Ala Pro

20 25 30

gga tot toa tac tgg aca gga ago tta ttt gta tac atg att acc act
44
Gly Ser Ser Tyr Trp Thr Gly Ser Leu Phe Val Tyr Met Ile Thr Thr
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aat aag tat aaa

56

Asn Lys Tyr Lys

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130588.00025.ST25.txt

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Gly Ser Ser Tyr Trp Thr Gly Ser Leu Phe Val Tyr Met Ile Thr Thr 35 40 45

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1 5 10 15

ggg ata tcc tcg ttc tat acg aaa gac tta atc gta atg ggt gca cca 96 Gly Ile Ser Ser Phe Tyr Thr Lys Asp Leu Ile Val Met Gly Ala Pro

20 25 30

gga tct tca tac tgg aca gga agc tta ttt gta tac atg att acc act 44 Gly Ser Ser Tyr Trp Thr Gly Ser Leu Phe Val Tyr Met Ile Thr Thr

Page 9

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1

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10

15

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60

Pro Thr Gly Gly

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Ser Tyr Trp Thr Gly Ser
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130588.00025.ST25.txt

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15 10 5 1

aca ttg ttt ggg tat agt tgg ctt cat agt cat gga gca cac aga tgg Thr Leu Phe Gly Tyr Ser Trp Leu His Ser His Gly Ala His Arg Trp

> 30 25 20

ctg cta gta ggc gca

Leu Leu Val Gly Ala

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Tyr Asn Val Asp Thr Glu Ser Ala Leu Leu Tyr Gln Gly Pro His Asn 15 10

Page 14

130588.00025.ST25.txt

Thr Leu Phe Gly Tyr Ser Trp Leu His Ser His Gly Ala His Arg Trp
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1 5 10 15

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20 25 30

aga acc gaa tta agt aag aga ata gcc cct ggt tat cag gac tac gtt 44 Arg Thr Glu Leu Ser Lys Arg Ile Ala Pro Gly Tyr Gln Asp Tyr Val

35 40 45

aaa aag ttc gga gag cat ttt gct agt tgc caa gca ggt atc agt agt 92 Lys Lys Phe Gly Glu His Phe Ala Ser Cys Gln Ala Gly Ile Ser Ser Page 15

1

130588.00025.ST25.txt

2

50 55 60

ttc tac act aag gat tta att gtc atg ggg gcg

25

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Arg Thr Glu Leu Ser Lys Arg Ile Ala Pro Gly Tyr Gln Asp Tyr Val 35 40 45

Lys Lys Phe Gly Glu His Phe Ala Ser Cys Gln Ala Gly Ile Ser Ser 50 55 60

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1 5 10 15

cag gtg aag cca gga agt tat tta ggg tat agt gta ggt gcc ggc cat 96 Gln Val Lys Pro Gly Ser Tyr Leu Gly Tyr Ser Val Gly Ala Gly His

20 25 30

ttc aga agt caa cac acg aca gaa gtt gtc ggc ggt gca cca caa cat 44 Phe Arg Ser Gln His Thr Thr Glu Val Val Gly Gly Ala Pro Gln His

1

2

35 40 45

gag cag ata gga aaa gct tac atc ttt agt ata gat gaa aaa gaa tta 192 Glu Gln Ile Gly Lys Ala Tyr Ile Phe Ser Ile Asp Glu Lys Glu Leu

50 · 55 60

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65 70

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Phe Arg Ser Gln His Thr Thr Glu Val Val Gly Gly Ala Pro Gln His 35 40 45

Glu Gln Ile Gly Lys Ala Tyr Ile Phe Ser Ile Asp Glu Lys Glu Leu 50 55 60

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1 5 10 15

gat ggc ttc tca gac ctg ctc gtc ggt gct ccc atg caa tcg acg ata Page 18

96

Asp Gly Phe Ser Asp Leu Leu Val Gly Ala Pro Met Gln Ser Thr Ile 30 20 25 aga gaa gag ggt aga gtt ttt gtt tac atc aat tct gga agc ggg gca 1 Arg Glu Glu Gly Arg Val Phe Val Tyr Ile Asn Ser Gly Ser Gly Ala 35 40 45 gtt atg aac gca atg gag aca aac tta gtg gga agt gac aaa tac gca 1. Val Met Asn Ala Met Glu Thr Asn Leu Val Gly Ser Asp Lys Tyr Ala 60 55 50 qcq cga ttt ggg gaa tcc atc gtg aat ttg gga gat att gac aat gac 2 Ala Arg Phe Gly Glu Ser Ile Val Asn Leu Gly Asp Ile Asp Asn Asp 80 70 75 65 qqq ttt gaa gac gta gcg att gga gca cca cag gag gac gat ctc cag . 2 Gly Phe Glu Asp Val Ala Ile Gly Ala Pro Gln Glu Asp Asp Leu Gln 95 90 85

gga gct atc tat atc tac aac ggc aga gcg gat ggt ata tct tca aca 3

Gly Ala Ile Tyr Ile Tyr Asn Gly Arg Ala Asp Gly Ile Ser Ser Thr

100 105 110

ttt tcc caa aga att gag ggc cta caa ata tcg aag tcg cta tcc atg 84
Phe Ser Gln Arg Ile Glu Gly Leu Gln Ile Ser Lys Ser Leu Ser Met

115 120 125

130588.00025.ST25.txt ttt ggg cag agt att tct ggt cag atc gac gcg gat aac aat ggc tat Phe Gly Gln Ser Ile Ser Gly Gln Ile Asp Ala Asp Asn Asn Gly Tyr gtg gat gta gca gta ggc gcg ttc agg agt gat cgt agc gat tct gct Val Asp Val Ala Val Gly Ala Phe Arg Ser Asp Arg Ser Asp Ser Ala 160 · att tta tta aga acg cgt cca gtc gtc ata gtg gac gct tca ctt agt Val Leu Leu Arg Thr Arg Pro Val Val Ile Val Asp Ala Ser Leu Ser cat cct gaa tca gta aac cga aca aag ttt gat tgt gtc gag aat ggg His Pro Glu Ser Val Asn Arg Thr Lys Phe Asp Cys Val Glu Asn Gly tgg ccg agc gtg tgt ata gat ctg aca tta tgc ttc tcg tac aaa qqq Trp Pro Ser Val Cys Ile Asp Leu Thr Leu Cys Phe Ser Tyr Lys Gly aaq gaa gtt cct ggt tat att gta tta ttc tac aat atg agt ctt qat Lys Glu Val Pro Gly Tyr Ile Val Leu Phe Tyr Asn Met Ser Leu Asp gtt aac cgc aaa gcc gaa tcg cca ccg cgg ttt tat ttc agt agc aat Val Asn Arg Lys Ala Glu Ser Pro Pro Arg Phe Tyr Phe Ser Ser Asn

130588.00025.ST25.txt

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Gly Thr Ser Asp Val Ile Thr Gly Ser Ile Gln Val Ser Ser Arg Glu
245
250
255

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Ala Asn Cys Arg Thr His Gln Ala Phe Met Arg Lys Asp Val Arg Asp
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265
270

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Asp Gly Phe Ser Asp Leu Leu Val Gly Ala Pro Met Gln Ser Thr Ile 20 25 30

Arg Glu Glu Gly Arg Val Phe Val Tyr Ile Asn Ser Gly Ser Gly Ala 35 40 45

Val Met Asn Ala Met Glu Thr Asn Leu Val Gly Ser Asp Lys Tyr Ala 50 55 60

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Phe	Ser	Gln 115	Arg	Ile	Glu	Gly	Leu 120	Gln	Ile	Ser	Lys	Ser 125	Leu	Ser	Met
Phe	Gly 130	Gln	Ser	Ile	Ser	Gly 135	Gln	Ile	Asp	Ala	Asp 140	Asn	Asn	Gly	Tyr
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Val	Leu	Leu	Arg	Thr 165	Arg	Pro	Val	Val	Ile 170	Val	Asp	Ala	Ser	Ьеи 175	Ser
His	Pro	Glu	Ser 180	Val	Asn	Arg	Thr	Lys 185	Phe	Asp	Cys	Val	Glu 190	Asn	Gly
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Val 225	Asn	Arg	Lys	Ala	Glu 230	Ser	Pro	Pro	Arg	Phe 235	Tyr	Phe	Ser	Ser	Asn 240
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245

250

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130588.00025.ST25.txt

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<212> DNA

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<400> 31

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1 5 10 15

gaa ttt tcg gga gac gac aca gaa gat ttt gta gct ggg gtg ccc aaa 96 Glu Phe Ser Gly Asp Asp Thr Glu Asp Phe Val Ala Gly Val Pro Lys

20 25 30

ggg aat ttg act tat ggc tac gtt acc ata cta aat ggt tct gat att

Gly Asn Leu Thr Tyr Gly Tyr Val Thr Ile Leu Asn Gly Ser Asp Ile

35 40 45

cgt agt tta tat aat ttc agt ggg gag caa atg gca agc tat ttc gga 192 Arg Ser Leu Tyr Asn Phe Ser Gly Glu Gln Met Ala Ser Tyr Phe Gly

tat 40	gcg	gta	gca	gcg	acc	gac	gtc	aac	ggt	gat	999	ctg	gac	gat	ttg	2
	Ala	Val	Ala	Ala	Thr	Asp	Val	Asn	Gly	Asp	Gly	Leu	Asp	Asp	Leu	
65					70					75	•	•	٠		80	
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88	_	999								•						2
Leu	Val	Gly	Ala	Pro	Leu	Leu	Met	Asp	Arg	Thr	Pro	·Asp	Gly	Arg	Pro	
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			~~ +	aat	at à	tat	ata	taa	++-	a a a	a a c	CCS	ac a	aat	ata	3
36	_	gtg														J
Gln	Glu	Val	Gly	Arg	Val	Tyr	Val	Tyr	Leu	GIn	His	Pro	Ala	GIY	lie	
			100					105					110			
asa	cca	aca	cca	act	tta	acq	cta	acc	aas	cac	gac	gag	ttc	aac	caa	3
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GLu	Pro	Thr	Pro	Thr	ьeu	Inr		THY	GTÀ	HIS	Asp		Pne	GTÀ	Arg	
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	130					135					140					
aat	gac	gtt	gct	att	999	gca	cca	ttt	ggt	ggc	gaa	acg	caa	caa	ggt	4
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145	F				150					155					160	
7.43					100					100						
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130588.00025.ST25.txt

				165					170					175		
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Phe	Gly	Ser	Ala	Leu	Arg	Gly	Gly	Arg	Asp	Leu	Asp	Gly	Asn	Gly	Tyr	
		195					200					205				
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72		_														0
Pro	Asp	Leu	ile	vaı	Gly		Pne	GIA	vai	Asp		Ата	vaı	vai	Tyr	•
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225	1	2			230					235					240	
223					250					233					210	
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68 Ala	Met	Phe	Asn	Pro	Glu	Glu	Arg	Ser	Cys	Ser	 Leu	Glu	Gly	Asn	Pro	
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gtc 16	gcg	tgt	atc	aac	ctc	tcc	ttc	tgt	tta	aac	gca	tcg	gġt	aaa	cat	8
	Ala	Cys	Ile	Asn	Leu	Ser	Phe	Cys	Leu	Asn	Ala	Ser	Gly	Lys	His	
			260					265					270			
gtg 64	gct	gat	tcg	atc	gga	ttt	aca	gta	gaa	ctt	caa	cta	gat	tgg	cag	8

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9

10

Val Ala Asp Ser Ile Gly Phe Thr Val Glu Leu Gln Leu Asp Trp Gln

275 280 285

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Lys Gln Lys Gly Gly Val Arg Arg Ala Leu Phe Leu Ala Ser Arg Gln

290 295 300

gcg act tta aca caa acc cta ctg ata cag aac gga gcc aga gag gat 9

Ala Thr Leu Thr Gln Thr Leu Leu Ile Gln Asn Gly Ala Arg Glu Asp

305 310 315 320

tgc cgc gaa atg aag atc tac ctg aga aat gaa tct gag ttc cga gac 10

Cys Arg Glu Met Lys Ile Tyr Leu Arg Asn Glu Ser Glu Phe Arg Asp

325 330 335

aag tta tct ccg att cat att gct.

32

Lys Leu Ser Pro Ile His Ile Ala

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130588.00025.ST25.txt

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Gly Asn Leu Thr Tyr Gly Tyr Val Thr Ile Leu Asn Gly Ser Asp Ile 35 40 45

Arg Ser Leu Tyr Asn Phe Ser Gly Glu Gln Met Ala Ser Tyr Phe Gly 50 55 60

Tyr Ala Val Ala Ala Thr Asp Val Asn Gly Asp Gly Leu Asp Asp Leu 65 70 75 80

Leu Val Gly Ala Pro Leu Leu Met Asp Arg Thr Pro Asp Gly Arg Pro 85 90 95

Gln Glu Val Gly Arg Val Tyr Val Tyr Leu Gln His Pro Ala Gly Ile 100 105 110

Glu Pro Thr Pro Thr Leu Thr Leu Thr Gly His Asp Glu Phe Gly Arg 115 120 125

Phe Gly Ser Ser Leu Thr Pro Leu Gly Asp Leu Asp Gln Asp Gly Tyr 130 135 140

Asn Asp Val Ala Ile Gly Ala Pro Phe Gly Gly Glu Thr Gln Gly 145 150 155 160

Val Val Phe Val Phe Pro Gly Gly Pro Gly Gly Leu Gly Ser Lys Pro 165 170 175

Ser Gln Val Leu Gln Pro Leu Trp Ala Ala Ser His Thr Pro Asp Phe 180 185 190

Phe Gly Ser Ala Leu Arg Gly Gly Arg Asp Leu Asp Gly Asn Gly Tyr 195 200 205

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Pro Asp Leu Ile Val Gly Ser Phe Gly Val Asp Lys Ala Val Val Tyr 210 215 220

Arg Gly Gly Pro Ile Val Ser Ala Ser Ala Ser Leu Thr Ile Phe Pro 225 230 235 240

Ala Met Phe Asn Pro Glu Glu Arg Ser Cys Ser Leu Glu Gly Asn Pro 245 250 255

Val Ala Cys Ile Asn Leu Ser Phe Cys Leu Asn Ala Ser Gly Lys His
260 265 270

Val Ala Asp Ser Ile Gly Phe Thr Val Glu Leu Gln Leu Asp Trp Gln 275 280 285

Lys Gln Lys Gly Gly Val Arg Arg Ala Leu Phe Leu Ala Ser Arg Gln 290 295 300

Ala Thr Leu Thr Gln Thr Leu Leu Ile Gln Asn Gly Ala Arg Glu Asp 305 310 315 320

Cys Arg Glu Met Lys Ile Tyr Leu Arg Asn Glu Ser Glu Phe Arg Asp 325 330 335

Lys Leu Ser Pro Ile His Ile Ala 340

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aca 96	gaa	gac	ttt	gtt	gca	ggg	gtg	cct	aag	ggg	aat	cta	aca	tat	999	
	Glu	Asp	Phe	Val	Ala	Gly	Val	Pro	Lys	Gly	Asn	Leu	Thr	Tyr	Gly	
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	Val	Thr	Ile	Leu	Asn	Gly	Ser	Asp	Ile	Arg	Ser	Leu	Tyr	Asn	Phe	
		35					40					45				
tcc 92	ggt	gag	caa	atg	gcc	tca	tat	ttt	gga	tac	gcc	gtt	gcg	gct	acg	1
	Gly	Glu	Gln	Met	Ala	Ser	Tyr	Phe	Gly	Tyr	Ala	Val	Ala	Ala	Thr	
	50					55					60					
gac 40	gtt	aac	ggt	gac	gga	tta	gac	gat	ctt	ctt	gtg	gga	gct	CCC	ctg	2
	Val	Asn	Gly	Asp	Gly	Leu	Asp	Asp	Leu	Leu	Val	Gly	Ala	Pro	Leu	
65					70					75					80	
ctg 88	atg	gac	cga	acc	cct	gat	ggt	aga	ccc	cag	gaa	gtc	gga	aga	gtc	2
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tac 36	gtc	tac	ttg	caa	cat	CCC	gcc	ggc	ata	gaa	cca	acg	cca	act	tta.	3
	Val	Tyr	Leu	Gln	His	Pro	Ala	Gly	Ile	Glu	Pro	Thr	Pro	Thr	Leu	

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act ctc act ggg cat gac gaa ttt ggt aga ttc ggt tcc tct tta acc Thr Leu Thr Gly His Asp Glu Phe Gly Arg Phe Gly Ser Ser Leu Thr cct ctt ggc gac ttg gac cag gat gga tat aat gat gtg gca ata ggc Pro Leu Gly Asp Leu Asp Gln Asp Gly Tyr Asn Asp Val Ala Ile Gly gcg ccg ttt ggg ggg gag acc cag caa ggc gtg gtg ttc gtc ttt cca Ala Pro Phe Gly Glu Thr Gln Gln Gly Val Val Phe Val Phe Pro ggt gga ccg ggt ggg cta ggg tct aaa cca tca caa gtt tta caq cca Gly Gly Pro Gly Gly Leu Gly Ser Lys Pro Ser Gln Val Leu Gln Pro tta tgg gca gcg agt cac acg cca gat ttt ttc ggc agt gca ctc agg Leu Trp Ala Ala Ser His Thr Pro Asp Phe Phe Gly Ser Ala Leu Arg ggt gga cgg gac ttg gac ggc aac ggc tat ccg gat ctg ata gta ggg Gly Gly Arg Asp Leu Asp Gly Asn Gly Tyr Pro Asp Leu Ile Val Gly teg tte ggt gta gat aaa gea gta gte tat ege ggg

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Ser Phe Gly Val Asp Lys Ala Val Val Tyr Arg Gly

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210 215 220

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Tyr Val Thr Ile Leu Asn Gly Ser Asp Ile Arg Ser Leu Tyr Asn Phe 35 40 45

Ser Gly Glu Gln Met Ala Ser Tyr Phe Gly Tyr Ala Val Ala Ala Thr 50 55 60

Asp Val Asn Gly Asp Gly Leu Asp Asp Leu Leu Val Gly Ala Pro Leu 65 70 75 80

Leu Met Asp Arg Thr Pro Asp Gly Arg Pro Gln Glu Val Gly Arg Val 85 90 95

Tyr Val Tyr Leu Gln His Pro Ala Gly Ile Glu Pro Thr Pro Thr Leu 100 105 110

Thr Leu Thr Gly His Asp Glu Phe Gly Arg Phe Gly Ser Ser Leu Thr
115 120 125

Pro Leu Gly Asp Leu Asp Gln Asp Gly Tyr Asn Asp Val Ala Ile Gly
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130

Ala Pro Phe Gly Gly Glu Thr Gln Gln Gly Val Val Phe Val Phe Pro 145 150 155 160

Gly Gly Pro Gly Gly Leu Gly Ser Lys Pro Ser Gln Val Leu Gln Pro 165 170 175

Leu Trp Ala Ala Ser His Thr Pro Asp Phe Phe Gly Ser Ala Leu Arg 180 185 190

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Ser Phe Gly Val Asp Lys Ala Val Val Tyr Arg Gly 210 215 220

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1 5 10 15

acg gaa aaa gaa ccc tta tct gat ccg gtc ggg acg tgt tat tta tcg 96 Thr Glu Lys Glu Pro Leu Ser Asp Pro Val Gly Thr Cys Tyr Leu Ser

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ttc	agt	tgg	gca	gcg	ggt	caa	999	tat	tgc	caa	ggc	ggc	ttc	agt	gcc		1
92 Phe	Ser	Trp	Ala	Ala	Gly	Gln	Gly	Tyr	Cys	Gln	Gly	Gly	Phe	Ser	Ala		
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40 Glu	Phe	Thr	Lys	Thr	Gly	Arg	Val	Val	Leu	Gly	Gly	Pro	Gly	Ser	Tyr		
65					70					75					80		
					a++	ata	taa	gat	202	022	asa	asa	at a		asa		2
·88								gct									۷.
Phe	Trp	Gin	GIY		11e	ьeu	ser	Ala		GTII	GIU	GIII	TTG		GIU		
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120

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Thr Asp Asn Phe Thr Arg Ile Leu Glu Tyr Ala Pro Cys Arg Ser Asp 35 40 45

Phe Ser Trp Ala Ala Gly Gln Gly Tyr Cys Gln Gly Gly Phe Ser Ala 50 55 60

Glu Phe Thr Lys Thr Gly Arg Val Val Leu Gly Gly Pro Gly Ser Tyr 65 70 75 80

Phe Trp Gln Gly Gln Ile Leu Ser Ala Thr Gln Glu Gln Ile Ala Glu 85 90 95

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Gly Val Asp Val Asp Gln Asp Gly Glu Thr Glu Leu Ile Gly Ala Pro
                                                          15
                                     10
1
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tta ttt tat ggt gaa caa aga ggg 72 Leu Phe Tyr Gly Glu Gln Arg Gly

20

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ata aca gat gga gaa gca aca gac agt gga caa att gat gca gca aaa

Ile Thr Asp Gly Glu Ala Thr Asp Ser Gly Gln Ile Asp Ala Ala Lys

1 5 10 15

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130588.00025.ST25.txt
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10

Ile Thr Asp Gly Glu Ala Thr Ser Gly Cys

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1

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130588.00025.ST25.txt

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Pro Ile Thr Gln Leu Leu Gly Arg Thr His Thr Ala Thr Gly Ile Arg
                                    10
                                                         15
                5
1
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aaa

130588.00025.ST25.txt

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51
Lys
       52
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                5 .
                                     10
                                                          15
1
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aga 51

15

130588.00025.ST25.txt

Arg

1

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gga agt ata atc cca cat gac ttt 72 Gly Ser Ile Ile Pro His Asp Phe

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10

20

Lys Ser Lys Thr Leu Phe Ser

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48
Phe Arg Arg Met Lys Glu Phe Val Ser Thr Val Met Glu Gln Leu Lys
                5
1
                                     10
                                                          15
aaa agt aag aca tta ttc agt
```

54

Arg Glu

130588.00025.ST25.txt

20.

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58
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                                     10
                                                         15
gaa gca gga gaa agt gta agt ttt caa tta caq ata
Glu Ala Gly Glu Ser Val Ser Phe Gln Leu Gln Ile
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                                25
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                5
                                     10
                                                          15
tgg aga
54
Trp Arg
```

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1

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1 5 10 15

aga cca ctg gat caa ttt gtg tta caa agt cat gct tgg ttc aat gtt 96

Arg Pro Leu Asp Gln Phe Val Leu Gln Ser His Ala Trp Phe Asn Val

20 25 30

agt agt tta cca tac gcg gta

17

Ser Ser Leu Pro Tyr Ala Val

35

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Arg Pro Leu Asp Gln Phe Val Leu Gln Ser His Ala Trp Phe Asn Val 20 25 30

Ser Ser Leu Pro Tyr Ala Val 35

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33
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1
                5
                                     10
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130588.00025.ST25.txt

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	Leu	Gly	Ala	Pro	Ser	Leu	Leu	Leu	Thr	Gly	Thr	Gln	Leu	Tyr	Gly		
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aga 84	ttc	gga	tct	gca	ata	gcg	cca	ctc	999	gat	ttg	gat	aga	gat	ggc	:	3
	Phe	Gly	Ser	Ala	Ile	Ala	Pro	Leu	Gly	Asp	Leu	Asp	Arg	Asp	Gly		
		115					120			-		125	•				,
tat 32	aac	gat	ata	gct	gtg	gcc	gcc	cct	tac	gga	gga	CCC	tcc	ggc	aga	•	4
	Asn	Asp	Ile	Ala	Val	Ala	Ala	Pro	Tyr	Gly	Gly	Pro	Ser	Gly	Arg		
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80 999	cag	gtt	ctg	gtt	ttc	cta	999	caa	agt	gaa	999	tta	agg	tca	aga	4	4
	Gln	Val	Leu	Val	Phe	Leu	Gly	Gln	Ser	Glu	Gly	Leu	Arg	Ser	Arg		
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ccg 28	tct	caa	gtc	tta	gac	tcg	cca	ttt	cca	acc	gga	agt.	gcg	ttt	aaa	Ę	5
	Ser	Gln	Val	Leu	Asp	Ser	Pro	Phe	Pro	Thr	Gly	Ser	Aļa	Phe	Gly		
				165	•				170				٠	175			
ttc 76	agt	ctc	cgt	ggt	gca	gṫg	gac	atc	gat	gac	aat	ggt	tac	cċg	gat	5	5
	Ser	Leu	Arg	Gly	Ala [.]	Val	Asp	Ile	Asp	Asp	Asn	Gly	Tyr	Pro	Asp		
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cag ccc gta gtt aaa gct tca gtc caa ctg ctg ctg caa gac agc ctg
72
Gln Pro Val Val Lys Ala Ser Val Gln Leu Leu Leu Gln Asp Ser Leu
210
215
220

6

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Asn Pro Ala

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Gln Arg Leu His Arg Leu Arg Ala Glu Gln Met Ala Ser Tyr Phe Gly 35 40 45

His Ser Val Ala Val Thr Asp Val Asn Gly Asp Gly Arg His Asp Leu 50 55 60

Leu Val Gly Ala Pro Leu Tyr Met Glu Ser Arg Ala Asp Arg Lys Leu 70 75 80

Ala Glu Val Gly Arg Val Tyr Leu Phe Leu Gln Pro Arg Gly Pro His
Page 56

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85 90 95

Ala Leu Gly Ala Pro Ser Leu Leu Leu Thr Gly Thr Gln Leu Tyr Gly
100 105 110

Arg Phe Gly Ser Ala Ile Ala Pro Leu Gly Asp Leu Asp Arg Asp Gly 115 120 125

Tyr Asn Asp Ile Ala Val Ala Ala Pro Tyr Gly Gly Pro Ser Gly Arg 130 135 140

Gly Gln Val Leu Val Phe Leu Gly Gln Ser Glu Gly Leu Arg Ser Arg 145 150 155 160

Pro Ser Gln Val Leu Asp Ser Pro Phe Pro Thr Gly Ser Ala Phe Gly 165 170 175

Phe Ser Leu Arg Gly Ala Val Asp Ile Asp Asp Asn Gly Tyr Pro Asp 180 185 190

Leu Ile Val Gly Ala Tyr Gly Ala Asn Gln Val Ala Val Tyr Arg Ala 195 200 205

Gln Pro Val Val Lys Ala Ser Val Gln Leu Leu Gln Asp Ser Leu 210 215 220

Asn Pro Ala 225

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130588.00025.ST25.txt

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gca cca tta tat

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Ala Pro Leu Tyr

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<212> PRT

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Ala Pro Leu Tyr 20

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gga ggc tac tac ttc ctg ggg cta ctc gca cag gca ccc gtg gcg gac 96 Gly Gly Tyr Tyr Phe Leu Gly Leu Leu Ala Gln Ala Pro Val Ala Asp 20 25 30

ata ttc tcg tct tat aga cct ggg att ttg ttg tgg cac gtc tcc tct 1
44
Ile Phe Ser Ser Tyr Arg Pro Gly Ile Leu Leu Trp His Val Ser Ser
35
40
45

cag tot the agt the gat age age age cag tat the gad gga tae 192
Gln Ser Leu Ser Phe Asp Ser Ser Asn Pro Glu Tyr Phe Asp Gly Tyr
50 55 60

tgg ggg tat tct gtg gca gtc ggt gag ttc gat ggt gat ctg aat act 2
40
Trp Gly Tyr Ser Val Ala Val Gly Glu Phe Asp Gly Asp Leu Asn Thr
65 70 75 80

aca gaa tat gtg gta ggg gct cct aca tgg agt tgg act tta ggc gcg 288

Thr Glu Tyr Val Val Gly Ala Pro Thr Trp Ser Trp Thr Leu Gly Ala

85 90 95

gtc gag ata tta gat agc tac tac caa egc tta cac aga ttg egt get 36 .

						130	0588	.0002	25.S	Γ25.	txt					
Val	Glu	Ile	Leu	Asp	Ser							arg	Lev	a Arc	g Ala	
			100					105					110)		
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	Gln	Met	Ala	Ser	Tyr	Phe	Gly	His	Ser	Val	Ala	Val	Thr	Asp	Val	
		115					120					125				
aat 32	ggt	gat	gga	cġg	cat	gac	ctc	cta	gtt	gga	gct	cca	ctt	tac	atg	4
	Gly	Asp	Gly	Arg	His	Asp	Leu	Leu	Val	Gly	Ala	Pro	Leu	Tyr	Met	
	130					135	•				140					
gag 80	agc	aga	gcg	gac	cga	aag	tta	gct	gaa	gta	gga	aga	gtt	tat	ttg	4
	Ser	Arg	Ala	Asp	Arg	Lys	Leu	Ala	Glu	Val	Gly	Arg	Val	Tyr	Leu	
145					150	•				155					160	
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28 Phe	Leu	Gln	Pro	Arg	Gly	Pro	His	Ala	Leu	Gly	Ala	Pro	Ser	Leu	Leu	
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76 Leu	Thr	Gly	Thr	Gln	Leu	Tyr	Gly	Arg	Phe	Gly	Ser	Ala	Ile	Ala	Pro	
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					-											
	999	gac	ctt	gat	cgc	gac	gga	tat	aac	gac	atc	gca	gtt	gcc	gcg	6
24 Leu	Gly	Asp	Leu	Asp	Arg	Asp	Gly	Tyr	Asn	Asp	Ile	Ala	Val	Ala	Ala	
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							200					203				
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130588.00025.ST25.txt

72 Pro Tyr Gly Gly Pro Ser Gly Arg Gly Gln Val Leu Val Phe Leu Gly 215 220 210 caa aqt gaa qqc ctc cgt agt aga ccg agc cag gta ctg gac agt ccq Gln Ser Glu Gly Leu Arg Ser Arg Pro Ser Gln Val Leu Asp Ser Pro 230 225 235 240 7 tit ccc acq qqc tcq qct ttt ggt ttt tca tta aga ggt gcg gta gac Phe Pro Thr Gly Ser Ala Phe Gly Phe Ser Leu Arg Gly Ala Val Asp 245 250 255 ate gat gat aac gga tac eec gat etc ata gta ggg gee tat gge gee Ile Asp Asp Asn Gly Tyr Pro Asp Leu Ile Val Gly Ala Tyr Gly Ala 260 265 270 aac caq gtc gca gtt tat agg gcc cag cca gta gtg aaa gca tca gtc Asn Gln Val Ala Val Tyr Arg Ala Gln Pro Val Val Lys Ala Ser Val 275 280 285

caa tta cta gtt cag gac 8 82 Gln Leu Leu Val Gln Asp

290

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<220>

<223> Description of Artificial Sequence: Integrin

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Gly Gly Tyr Tyr Phe Leu Gly Leu Leu Ala Gln Ala Pro Val Ala Asp 20 25 30

Ile Phe Ser Ser Tyr Arg Pro Gly Ile Leu Leu Trp His Val Ser Ser 35 40 45

Gln Ser Leu Ser Phe Asp Ser Ser Asn Pro Glu Tyr Phe Asp Gly Tyr 50 55 60

Trp Gly Tyr Ser Val Ala Val Gly Glu Phe Asp Gly Asp Leu Asn Thr 65 70 75 80

Thr Glu Tyr Val Val Gly Ala Pro Thr Trp Ser Trp Thr Leu Gly Ala 85 90 95

Val Glu Ile Leu Asp Ser Tyr Tyr Gln Arg Leu His Arg Leu Arg Ala 100 105 110

Glu Gln Met Ala Ser Tyr Phe Gly His Ser Val Ala Val Thr Asp Val 115 120 125

Asn Gly Asp Gly Arg His Asp Leu Leu Val Gly Ala Pro Leu Tyr Met
130 135 140

Glu Ser Arg Ala Asp Arg Lys Leu Ala Glu Val Gly Arg Val Tyr Leu 145 150 155 160

Phe Leu Gln Pro Arg Gly Pro His Ala Leu Gly Ala Pro Ser Leu Leu 165 170 175

130588.00025.ST25.txt

Leu Thr Gly Thr Gln Leu Tyr Gly Arg Phe Gly Ser Ala Ile Ala Pro 180 185 190

Leu Gly Asp Leu Asp Arg Asp Gly Tyr Asn Asp Ile Ala Val Ala Ala 195 200 205

Pro Tyr Gly Gly Pro Ser Gly Arg Gly Gln Val Leu Val Phe Leu Gly 210 215 220

Gln Ser Glu Gly Leu Arg Ser Arg Pro Ser Gln Val Leu Asp Ser Pro 225 230 235 240

Phe Pro Thr Gly Ser Ala Phe Gly Phe Ser Leu Arg Gly Ala Val Asp 245 250 255

Ile Asp Asp Asn Gly Tyr Pro Asp Leu Ile Val Gly Ala Tyr Gly Ala 260 265 270

Asn Gln Val Ala Val Tyr Arg Ala Gln Pro Val Val Lys Ala Ser Val 275 280 285

Gln Leu Leu Val Gln Asp 290

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<211> 21

<212> DNA

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130588.00025.ST25.txt
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1
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       Xaa can be any naturally occurring amino acid
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Asp Xaa Xaa Xaa Xaa Asp Xaa Ser Xaa Ser Xaa Lys Asp Asp Leu .
                                                         15
                                     10
 1
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1				5					10					15		
•																
tga 96	gtc	tgc	ggc	caa	tgt	gta	tgc ·	cgg	aaa	cgt	gac	aac	aca	aac	gaa	
	Val	Cys	Gly	Gln	Cys	Val	Cys	Arg	Lys	Arg	Asp	Asn	Thr	Asn	Glu	
	,		20					25					30			
atc 44	tat	agt	gga	aag	ttt	tgt	gag	tgt	gat	aat	ttc	aac	tgt	gat	cgc	1
	Tyr	Ser	Gly	Lys	Phe	Cys	Glu	Cys	Asp	Asn	Phe	Asn	Cys	Asp	Arg	
		35					40					45				
				÷												
agc 92	aat	ggc	tta	ata	tgc	ggt	ggc	aat	gga	gtt	tgc	aag	tgt	agg	gtg	1
	Asn	Gly	Leu	Ile	Cys	Gly	Gly	Asn	Gly	Val	Cys	Lys	Cys	Arg	Val	
	50					55					60					
												•				
tgt 40	gaa	tgc ·	aat	cca	aat	tat	aca	aaa	agt	gca	tgc	gat	tgc	tct	tta	2
Cys	Glu	Cys	Asn	Pro	Asn	Tyr	Thr	Gly	Ser	Ala	Cys	Asp	Cys	Ser	Leu	
65					70 ·		•			75.					80	
gac [.] 88	act	agt	acg	tgc	gag	gca	tcc	aac	999	cag	ata	tgt	aat	gga	aga	2
	Thr	Ser	Thr	Cys	Glu	Ala	Ser	Asn	Gly	Gln	Ile	Cys	Aṡn	Gly	Arg	
				85					90					95		
								•								
ggt 24	att	tgt	gag	tgt	ggt	gta	tgc	aaa	tgt	acc	gac					3
	Ile	Cys	Glu	Cys	Gly	Val	Cys	Lys	Cys	Thr	Asp					

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Cys Val Cys Gly Gln Cys Val Cys Arg Lys Arg Asp Asn Thr Asn Glu 20 25 30

Ile Tyr Ser Gly Lys Phe Cys Glu Cys Asp Asn Phe Asn Cys Asp Arg 35 40 45

Ser Asn Gly Leu Ile Cys Gly Gly Asn Gly Val Cys Lys Cys Arg Val 50 . 60

Cys Glu Cys Asn Pro Asn Tyr Thr Gly Ser Ala Cys Asp Cys Ser Leu 70 75 80

Asp Thr Ser Thr Cys Glu Ala Ser Asn Gly Gln Ile Cys Asn Gly Arg 85 90 95

Gly Ile Cys Glu Cys Gly Val Cys Lys Cys Thr Asp

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130588.00025.ST25.txt
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21 -
Cys Thr Ser Glu Gln Asn Cys
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       Artificial Sequence
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130588.00025.ST25.txt 15 1 5 10

cgg gct gag gat tat cct atc gac ctt tac tat ctt atg gat ctc tca Arq Ala Glu Asp Tyr Pro Ile Asp Leu Tyr Tyr Leu Met Asp Leu Ser 25 30 20 tat agt atg aaa gat gat ctg gag aat gtt aag tcc tta ggg acc gat Tyr Ser Met Lys Asp Asp Leu Glu Asn Val Lys Ser Leu Gly Thr Asp 40 45 35 tta atg aac gag atg aga atc act tca gac ttc aga att gga ttt Leu Met Asn Glu Met Arg Arg Ile Thr Ser Asp Phe Arg Ile Gly Phe 50 55 60 ggc tct ttt gtc gaa aaa acc gta atg cca tac ata agc aca acc cca 2 Gly Ser Phe Val Glu Lys Thr Val Met Pro Tyr Ile Ser Thr Thr Pro 75 . 80 70 65 gca aag ctg agg aat ccg tgt aca tcg gag caa aac tgc act act ccc 2 Ala Lys Leu Arg Asn Pro Cys Thr Ser Glu Gln Asn Cys Thr Thr Pro 90 95 85

ttc agt tat aag aat gtt ctc agt ctg acg aac aaa ggg gaa gta ttt 3

Phe Ser Tyr Lys Asn Val Leu Ser Leu Thr Asn Lys Gly Glu Val Phe 100 105 110

aac gag cta gtg gga aaa cag aga att agc ggt aac ctc gac tct cca 3 Asn Glu Leu Val Gly Lys Gln Arg Ile Ser Gly Asn Leu Asp Ser Pro Page 70

130588.00025.ST25.txt

		115		13			120					125				
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	Gly	Gly	Phe	Asp	Ala	Ile	Met	Gln	Val	Ala	Val	Cys	Gly	Ser	Leu	
٠	130					135					140					
ata	aaa	taa	cat	aat	gta	act	aga	cha	t.ta	at.a	t.t.t.	t.cc	acc	gac	acc	4
80			_		Val											
145	Gry		nrg	ADII	150	1111	1129	Бей	Lea	155	1110			p	160	
143										133						
	ttc	cac	ttc	gct	gga	gac	ggc	aag	cta	999	gga	atc	gta	ttg	cct	5
28 Gly	Phe	His	Phe	Ala	Gly	Asp	Gly	Lys	Leu	Gly	Gly	Ile	Val	Leu	Pro.	
			•	165					170					175		
224	~>+	aat		taa	cat	tta	as s	aat	aat	ata	tat	200	, ata	tca	cac	5
76	_		_	-	His											J
ASN	Asp	СТА		Cys	HIS.	пец	Gru	•	ASII	Mec	TÀT	1111	190	261	urp	
			180					185					190			
	tac	gac	tac	сса	tcc	ata	gcc	cat	tta	gtc	caa	aag	ctg	agc	gaa	6
24 Tyr	Tyr	Asp	Tyr	Pro	Ser	Ile	Ala	His	Leu	Val	Gln	Lys	Leu	Ser	Glu	
		195					200					205				
			•									.			1	_
72					ata											6
Asn		Ile	Gln	Thr	Ile		Ala	Val	Thr	Glu		Phe	Gln	Pro	Val	
	210					215			-		220					
tat 08	aag	gag	ctt	aaa	aat	ctc	atc	ccg	aaa	tca	gcg					7

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Tyr Lys Glu Leu Lys Asn Leu Ile Pro Lys Ser Ala

.225 230 235

<210> 99

<211> 236 ·.

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Tyr Ser Met Lys Asp Asp Leu Glu Asn Val Lys Ser Leu Gly Thr Asp 35 40 45

Leu Met Asn Glu Met Arg Arg Ile Thr Ser Asp Phe Arg Ile Gly Phe 50 55 60

Gly Ser Phe Val Glu Lys Thr Val Met Pro Tyr Ile Ser Thr Thr Pro 65 70 75 80

Ala Lys Leu Arg Asn Pro Cys Thr Ser Glu Gln Asn Cys Thr Thr Pro 85 90 95

Phe Ser Tyr Lys Asn Val Leu Ser Leu Thr Asn Lys Gly Glu Val Phe 100 105 110

Asn Glu Leu Val Gly Lys Gln Arg Ile Ser Gly Asn Leu Asp Ser Pro 115 120 125

130588.00025.ST25.txt

Glu Gly Gly Phe Asp Ala Ile Met Gln Val Ala Val Cys Gly Ser Leu 130 135 140

Ile Gly Trp Arg Asn Val Thr Arg Leu Leu Val Phe Ser Thr Asp Ala 145 150 155 160

Gly Phe His Phe Ala Gly Asp Gly Lys Leu Gly Gly Ile Val Leu Pro 165 : 170 : 175

Asn Asp Gly Gln Cys His Leu Glu Asn Asn Met Tyr Thr Met Ser His 180 185 190

Tyr Tyr Asp Tyr Pro Ser Ile Ala His Leu Val Gln Lys Leu Ser Glu 195 200 205

Asn Asn Ile Gln Thr Ile Phe Ala Val Thr Glu Glu Phe Gln Pro Val 210 215 220

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<220>

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<220>

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<221> CDS

<222> (1)..(36)

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Asn Lys Gly Glu Val Phe Asn Glu Leu Val Gly Lys

5

10

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Asn Lys Gly Glu Val Phe Asn Glu Leu Val Gly Lys
                5
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                5
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Asp Tyr Pro Ile Asp Leu Tyr Tyr Leu Met Asp Leu Ser Tyr Ser Met 5 10 15

Lys Asp Asp Leu Glu Val Lys Ser Leu Gly Page 75

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Asn Val Lys Ser Leu Gly Thr Ala Leu Met Arg Glu Met Glu Lys Ile

1 5 10 15

aca agt gat ttt

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Thr Ser Asp Phe

20

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Thr Ser Asp Phe

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																•
36	_							tgc								3
Pro	Cys	Pro	Asn	Lys	Glu	ГÀЗ	Glu	Суѕ	Gln	Pro	Pro	Phe	Ala	Phe	Arg	
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76								att								5
Ala	Gly	Asp	Gly	Lys	Leu	Gly		Ile		Thr	Pro	Asn	Asp	Gly	Arg	
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130588.00025.ST25.txt

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	Ile	Phe	Ala	Val	Thr	Ser	Arg	Met	Val	Lys	Thr	Tyr	Glu	Lys	Leu		
225					230		•			235					240		
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44	-	atc		٠			_									7	
Thr	Glu	Ile	Ile	Pro	Lys	Ser	Ala										
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Gly Gln Ala Ala Ala Phe Asn Val Thr Phe Arg Arg Ala Lys Gly Tyr

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20.

30

Pro Ile Asp Leu Tyr Tyr Leu Met Asp Leu Ser Tyr Ser Met Leu Asp 35 40 45

Asp Leu Arg Asn Val Lys Leu Gly Gly Asp Leu Leu Arg Ala Leu 50 · 55 60

Asn Glu Ile Thr Glu Ser Gly Arg Ile Gly Phe Gly Ser Phe Val Asp 65 70 75 80

Lys Thr Val Leu Pro Phe Val Asn Thr His Pro Asp Lys Leu Arg Asn 85 90 95

Pro Cys Pro Asn Lys Glu Lys Glu Cys Gln Pro Pro Phe Ala Phe Arg 100 105 110

His Val Leu Lys Leu Thr Asn Asn Ser Asn Gln Phe Gln Thr Glu Val

Gly Lys Gln Leu Ile Ser Gly Asn Leu Asp Ala Pro Glu Gly Gly Leu 130 135 140

Asp Ala Met Met Gln Val Ala Ala Cys Pro Glu Glu Ile Gly Trp Arg 145 150 155 160

Asn Val Thr Arg Leu Leu Val Phe Ala Thr Asp Asp Gly Phe His Phe 165 170 175

Ala Gly Asp Gly Lys Leu Gly Ala Ile Leu Thr Pro Asn Asp Gly Arg 180 185 190

Cys His Leu Glu Asp Asn Leu Tyr Lys Arg Ser Asn Glu Phe Asp Tyr 195 200 205

Pro Ser Val Gly Gln Leu Ala His Lys Leu Ala Glu Asn Asn Ile Gln Page 80

130588.00025.ST25.txt 215 220

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gac gat cta cgt aac gtt aag aaa ctt gga ggt gat tta cta aga gct 96 Asp Asp Leu Arg Asn Val Lys Lys Leu Gly Gly Asp Leu Leu Arg Ala

20 . 25 30

ctt aac gaa atc acg gag agt ggg cga atc ggc ttc ggc tca ttc gtc 44 Leu Asn Glu Ile Thr Glu Ser Gly Arg Ile Gly Phe Gly Ser Phe Val

35 40 45

gac aag aca gta ttg ccc ttc gta aac acg cac cca gac aag ctt aga 192

Asp	Lys	Thr	Val	Leu	Pro			Asn			Pro	Asp.	Lys	Leu	Arg	
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40											ccc.					2
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76										Lys							
1 Y	т г	10	OCI	180					185	-1-				190			
				100											-		
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+ +		00	asa	ata	att.	cca	222	tct	act	gtg	aac	aaa	ctc	tcc	gaa	gat.	6
72										Val							
ьe			GIU	116	116	FIO	215	per	лта	val	Gry	. 220	БСС	501	O_u	p	
	۷	10					213					220					
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130588.00025.ST25.txt

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Leu Asn Glu Ile Thr Glu Ser Gly Arg Ile Gly Phe Gly Ser Phe Val 35 40 45

Asp Lys Thr Val Leu Pro Phe Val Asn Thr His Pro Asp Lys Leu Arg 50 55 60

Asn Pro Cys Pro Asn Lys Glu Lys Glu Cys Gln Pro Pro Phe Ala Phe 65 70 75 80

Arg His Val Leu Lys Leu Thr Asn Asn Ser Asn Gln Phe Gln Thr Glu 85 90 95

Val Gly Lys Gln Leu Ile Ser Gly Asn Leu Asp Ala Pro Glu Gly Gly
100 105 110

Leu Asp Ala Met Met Gln Val Ala Ala Cys Pro Glu Glu Ile Gly Trp 115 120 125

Arg Asn Val Thr Arg Leu Leu Val Phe Ala Thr Asp Asp Gly Phe His
130 135 140

Phe Ala Gly Asp Gly Lys Leu Gly Ala Ile Leu Thr Pro Asn Asp Gly
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130588,00025.ST25.txt 160 150 · 155 145 Arg Cys His Leu Glu Asp Asn Leu Tyr Lys Arg Ser Asn Glu Phe Asp 170 165 Tyr Pro Ser Val Gly Gln Leu Ala His Lys Leu Ala Glu Asn Asn Ile 190 185 180 Gln Pro Ile Phe Ala Val Thr Ser Arg Met Val Lys Thr Tyr Glu Lys 200 195 Leu Thr Glu Ile Ile Pro Lys Ser Ala Val Gly Glu Leu Ser Glu Asp 220 215 210 Ser Ser Asn Val Val His Leu Ile Lys Asn Ala Tyr Asn Lys Leu Ser 240 235 230 225 Ser Arg Val Phe Leu Asp His Asn Ala Leu Pro Asp Thr Leu Lys Val 250 245 Thr Tyr Asp Ser Phe 260 <210> 112 <211> 15 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: Integrin <220> <221> CDS <222> (1)..(15) <400> 112 aga aat gta aaa aag Arg Asn Val Lys Lys

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130588.00025.ST25.txt
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Gly Gln Leu Ala His
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Glu Leu Ser Glu Asp Ser Ser Asn Val Val His Leu Ile Lys Asn Ala
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15 10 1 tat aac aaa cta agt tcg aga gtt ttc tta gac cac aat gca ctg cca 96 Tyr Asn Lys Leu Ser Ser Arg Val Phe Leu Asp His Asn Ala Leu Pro 30 25 20 gat acg ttg aag gta aca tac gac agc ttt tgc tcc aat ggg gtg acc 1 Asp Thr Leu Lys Val Thr Tyr Asp Ser Phe Cys Ser Asn Gly Val Thr 45 40 35 cat aga aac cag cca aga ggc gat tgt gac gga gta caa ata aat gta 1 His Arg Asn Gln Pro Arg Gly Asp Cys Asp Gly Val Gln Ile Asn Val 60 55 50 cca ata aca ttc cag gtt aag gtg aca gct act gag tgt ata caa gaa 2 Pro Ile Thr Phe Gln Val Lys Val Thr Ala Thr Glu Cys Ile Gln Glu 80 75 70 65 2 caa agt ttt gta att aga gcg ctt ggt 67 Gln Ser Phe Val Ile Arg Ala Leu Gly 85 <210> 121 <211> 89 PRT <212>

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Description of Artificial Sequence: Integrin

Artificial Sequence

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130588.00025.ST25.txt

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Tyr Asn Lys Leu Ser Ser Arg Val Phe Leu Asp His Asn Ala Leu Pro 20 25 30

Asp Thr Leu Lys Val Thr Tyr Asp Ser Phe Cys Ser Asn Gly Val Thr 35 40 45

His Arg Asn Gln Pro Arg Gly Asp Cys Asp Gly Val Gln Ile Asn Val 50 55 60

Pro Ile Thr Phe Gln Val Lys Val Thr Ala Thr Glu Cys Ile Gln Glu 65 70 75 80

Gln Ser Phe Val Ile Arg Ala Leu Gly 85

<210> 122

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1 5 10 , 15

aga tgt aga gat caa agt aga gac aga agt tta tgc cat gga aag ggc Page 90

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96

Arg Cys Arg Asp Gln Ser Arg Asp Arg Ser Leu Cys His Gly Lys Gly

20

25

30

1

ttt tta gaa tgt gga atc tgt aga tgc gat acg gga tat ata gga aaa 44 Phe Leu Glu Cys Gly Ile Cys Arg Cys Asp Thr Gly Tyr Ile Gly Lys

35

40

45

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20 25 30

Phe Leu Glu Cys Gly Ile Cys Arg Cys Asp Thr Gly Tyr Ile Gly Lys 35 40 45

Asn Cys Glu Cys Gln Thr Gln Gly 50 55

<210> 124

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130588.00025.ST25.txt

gca aga aaa aat 60 Ala Arg Lys Asn

20

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1 10 15

Ala Arg Lys Asn 20

127

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Asp Leu Ser Tyr Ser Leu Asp Asp Leu Arg Asn Val Lys Lys Leu Gly

1 5 . 10 15

gga gac cta tta aga gca ttg aac gaa

75

Gly Asp Leu Leu Arg Ala Leu Asn Glu

20 25

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1 5 10 15

Gly Asp Leu Leu Arg Ala Leu Asn Glu 20 25

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<212> DNA

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130588.00025.ST25.txt

48
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1 5 10 15

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Lys Asp Asp Leu Trp Ser Ile Gln Asn Leu Gly Thr Lys Leu Ala Thr
20 25 30

caa atg aga aag ctg aca tcg aat tta aga ata gga ttt gga gca ttc 1
44
Gln Met Arg Lys Leu Thr Ser Asn Leu Arg Ile Gly Phe Gly Ala Phe
35
40
45

gta gat aaa cca gta agc cct tat atg tat atc tct cca ccg gaa 189
Val Asp Lys Pro Val Ser Pro Tyr Met Tyr Ile Ser Pro Pro Glu
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1 10 15

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Gln Met Arg Lys Leu Thr Ser Asn Leu Arg Ile Gly Phe Gly Ala Phe 35 40 45

130588.00025.ST25.txt

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130588.00025.ST25.txt

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Phe Ser Ile Gln Val Arg Gln Val Glu Asp Tyr Pro Val Asp Ile Tyr

1 5 10 15

tac tta atg gac tta agc tat agt atg aag gac gat ctc tgg agt ata 96

Tyr Leu Met Asp Leu Ser Tyr Ser Met Lys Asp Asp Leu Trp Ser Ile

20 25 30

caa aat tta ggt acc aag ttg gcc acc caa atg cgt aaa tta act tca 144

Gln Asn Leu Gly Thr Lys Leu Ala Thr Gln Met Arg Lys Leu Thr Ser

35 40 45

aat tta cgg ata gga ttc ggg gca ttt gtg gat aaa ccc gta tcg ccg 1 92

Asn Leu Arg Ile Gly Phe Gly Ala Phe Val Asp Lys Pro Val Ser Pro

50 55 60

tac atg tat att agt cca cct gag gcg ctt gaa aac ccc tgc tac gac 2

Tyr Met Tyr Ile Ser Pro Pro Glu Ala Leu Glu Asn Pro Cys Tyr Asp

65 70 75 80

atg aaa aca acg tgt ctg cct atg ttt ggc tac aag cat gtc cta aca 288

Met Lys Thr Thr Cys Leu Pro Met Phe Gly Tyr Lys His Val Leu Thr

95

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130588.00025.ST25.txt

	acg	gat	caa	gtc	act	agg	ttc	aac	gag	gaa	gtt	aaa	aag	cag	agt	3
36 Leu	Thr	Asp	Gln	Val	Thr	Arg	Phe	Asn	Glu	Glu	Val	Lys	Lys	Gln	Ser	
			100					105					110			

gtg tct cgc aat aga gat gct ccg gaa

63

Val Ser Arg Asn Arg Asp Ala Pro Glu

115

120

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135

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Phe Ser Ile Gln Val Arg Gln Val Glu Asp Tyr Pro Val Asp Ile Tyr 1 5 10 15

Tyr Leu Met Asp Leu Ser Tyr Ser Met Lys Asp Asp Leu Trp Ser Ile 20 25 30

Gln Asn Leu Gly Thr Lys Leu Ala Thr Gln Met Arg Lys Leu Thr Ser 35 40 45

Asn Leu Arg Ile Gly Phe Gly Ala Phe Val Asp Lys Pro Val Ser Pro 50 55 60

Tyr Met Tyr Ile Ser Pro Pro Glu Ala Leu Glu Asn Pro Cys Tyr Asp 65 70 75 80

Met Lys Thr Thr Cys Leu Pro Met Phe Gly Tyr Lys His Val Leu Thr Page 98

130588.00025.ST25.txt

90 95

Leu Thr Asp Gln Val Thr Arg Phe Asn Glu Glu Val Lys Lys Gln Ser 100 105 110

Val Ser Arg Asn Arg Asp Ala Pro Glu 115 120

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1 ' 5 10 15

tgg tgc agt gat gaa gca tta cca tta gga agt cca aga 87

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20 25

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130588.00025.ST25.txt

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Trp Cys Ser Asp Glu Ala Leu Pro Leu Gly Ser Pro Arg 20 25

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Val Leu Glu Asp Arg Pro Leu Ser Asp Lys Gly Ser Gly Asp Ser Ser

1 5 10 . 15

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63

Gln Val Thr Gln Val

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Gln Val Thr Gln Val 20

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Asn Ile Asn Leu Ile Phe Ala Val Thr Glu Asn Val Val Asn Leu Tyr

1

5

10

15

cag aac tat agt gag cta ata cca gga aca aca gta gga gtt ctc agt 96

Gln Asn Tyr Ser Glu Leu Ile Pro Gly Thr Thr Val Gly Val Leu Ser

20

25

30

atg gat agt agt aat gta ctg caa ttg att gta gac gca tat gga aaa 44

Met Asp Ser Ser Asn Val Leu Gln Leu Ile Val Asp Ala Tyr Gly Lys

35

40

45

ata aga agt

53

Ile Arg Ser

1

130588.00025.ST25.txt

50

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                                                      30
            20
Met Asp Ser Ser Asn Val Leu Gln Leu Ile Val Asp Ala Tyr Gly Lys
                                                  45
                             40
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Ile Arg Ser
    50
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Ile Gly Phe Gly Ala Phe Val Asp Lys Pro Val Ser Pro Tyr Met Tyr
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130588.00025.ST25.txt

1

1 5 10 15

ata agt cca ccc gaa gca tta gag aat cca tgc tac gat atg aag aca 96 Ile Ser Pro Pro Glu Ala Leu Glu Asn Pro Cys Tyr Asp Met Lys Thr

20 25 30

aca tgt tta ccg atg ttt gga tat aaa 23 Thr Cys Leu Pro Met Phe Gly Tyr Lys

35 40

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<211> 41

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Thr Cys Leu Pro Met Phe Gly Tyr Lys
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130588.00025.ST25.txt

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1
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                                     10
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130588.00025.ST25.txt

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1
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130588.00025.ST25.txt

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130588.00025.ST25.txt

gac gaa aaa ata ggê tgg aga aac gat gca agt cac ctc ctt gtc ttc 96 Asp Glu Lys Ile Gly Trp Arg Asn Asp Ala Ser His Leu Leu Val Phe 20 25 30

aca acc gat gca aaa aca cat att gcc ctg gac ggg aga ttg gcc ggc

44

Thr Thr Asp Ala Lys Thr His Ile Ala Leu Asp Gly Arg Leu Ala Gly

35

40

45

ata gtt caa cca aat gat ggt cag tgt cat gta gga tca gac aat cac 1
92
Ile Val Gln Pro Asn Asp Gly Gln Cys His Val Gly Ser Asp Asn His
50
55
60

tat tot got ago act acg atg gat tac coa too tta gga tta atg aca 2
40
Tyr Ser Ala Ser Thr Thr Met Asp Tyr Pro Ser Leu Gly Leu Met Thr
65 70 75 80

gag aag cta tcg cag aag 58 Glu Lys Leu Ser Gln Lys

85

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Asp Ala Pro Glu Gly Gly Phe Asp Ala Ile Met Gln Ala Thr Val Cys Page 108

130588.00025.ST25.txt

15

1 5 10

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Thr Thr Asp Ala Lys Thr His Ile Ala Leu Asp Gly Arg Leu Ala Gly 35 40 45

Ile Val Gln Pro Asn Asp Gly Gln Cys His Val Gly Ser Asp Asn His 50 55 60

Tyr Ser Ala Ser Thr Thr Met Asp Tyr Pro Ser Leu Gly Leu Met Thr 65 70 75 80

Glu Lys Leu Ser Gln Lys 85

<210> 156

<211> 42

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atg gac tta agt tat agt atg aaa gat gat tta tgg agt ata 42

Met Asp Leu Ser Tyr Ser Met Lys Asp Asp Leu Trp Ser Ile

1 5 10

<210> 157

<211> 14

<212> PRT

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130588.00025.ST25.txt
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Gly Pro Asn Ile Cys Thr
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1
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Gly Pro Asn Ile Cys Thr
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130588.00025.ST25.txt
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Gly Pro Asn Ile Cys Thr Thr Arg Gly Val Ser Ser Cys
                5
                                    10
1
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Gly Pro Asn Ile Cys Thr Thr Arg Gly Val Ser Ser Cys
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Lys Asp Ser Leu Ile Val Gln Val Thr Phe Asp Cys Asp Cys Ala Cys Page 112 5

130588.00025.ST25.txt

1

10

15

15

Gln Ala Gln Ala Glu Pro Asn Ser His Arg Cys Asn Asn Gly Asn Gly 25 20

Thr Phe Glu Cys Gly Val Cys Arg Cys Gly Pro Gly Trp Leu Gly Ser 45 40 35

Gln Cys Glu Cys Ser Glu Glu Asp Tyr Arg Pro Ser Gln Gln Asp Glu

Cys Ser Pro Arg Glu 65

<210> 164

<211> 267

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10

1

aaa aaa ttt gac cgt gag ccc tat atg aca gaa aat act tgc aac agg Lys Lys Phe Asp Arg Glu Pro Tyr Met Thr Glu Asn Thr Cys Asn Arg

> 25 30 20

tat tgt aga gat gaa ata gag agc gtt aaa gag tta aaa gat aca ggt Page 113

130588.00025.ST25.txt

44
Tyr Cys Arg Asp Glu Ile Glu Ser Val Lys Glu Leu Lys Asp Thr Gly
35
40
45

aaa gat gca gtt aac tgt aca tat aaa aat gag gac gat tgt gtg gta 92
Lys Asp Ala Val Asn Cys Thr Tyr Lys Asn Glu Asp Asp Cys Val Val
50 55 60

cga ttc caa tat tat gaa gac agt tca gga aaa tct ata ttg tat gta
40
Arg Phe Gln Tyr Tyr Glu Asp Ser Ser Gly Lys Ser Ile Leu Tyr Val
65
70
75
80

gtg gaa gag cca gaa tgt cca aaa ggg 67 Val Glu Glu Pro Glu Cys Pro Lys Gly

85

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<211> 89

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Lys Lys Phe Asp Arg Glu Pro Tyr Met Thr Glu Asn Thr Cys Asn Arg 20 25 30

Tyr Cys Arg Asp Glu Ile Glu Ser Val Lys Glu Leu Lys Asp Thr Gly 35 40 45

130588.00025.ST25.txt

Lys Asp Ala Val Asn Cys Thr Tyr Lys Asn Glu Asp Asp Cys Val Val 50 55 60

Arg Phe Gln Tyr Tyr Glu Asp Ser Ser Gly Lys Ser Ile Leu Tyr Val 65 70 75 80

Val Glu Glu Pro Glu Cys Pro Lys Gly 85

<210> 166

<211> 15

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<223> Description of Artificial Sequence: Integrin

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<221> CDS

<222> (1)..(15)

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15

Lys Asp Asp Leu Trp

1

<210> 167

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Lys Asp Asp Leu Trp 5

168

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                                    10
1
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                                    10
                5
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1 5 10 15

cca agt ctg ggc tta atg aca gag aag tta agc caa aag aat tta aac 96 Pro Ser Leu Gly Leu Met Thr Glu Lys Leu Ser Gln Lys Asn Leu Asn

20 25 30

ttg atc ttt gca gtt aca gag aac gta gtc aat ctt tac cag aat tac 44 Leu Ile Phe Ala Val Thr Glu Asn Val Val Asn Leu Tyr Gln Asn Tyr

35 40 45

agt gag cta att cca gga acg acc gta gga gta ttg tcg atg gat agt 1
92
Ser Glu Leu Ile Pro Gly Thr Thr Val Gly Val Leu Ser Met Asp Ser
50
55
60

tca aat gtc ctc caa cta ata gtg gat gca tat ggt aaa ata aga agt 2
40
Ser Asn Val Leu Gln Leu Ile Val Asp Ala Tyr Gly Lys Ile Arg Ser
65 70 75 80

aaa gtt gaa tta gaa gta aga gat ctc cca 2
70
Lys Val Glu Leu Glu Val Arg Asp Leu Pro

85 90

<21.0> 171

130588.00025.ST25.txt

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Leu Ile Phe Ala Val Thr Glu Asn Val Val Asn Leu Tyr Gln Asn Tyr 35 40 45

Ser Glu Leu Ile Pro Gly Thr Thr Val Gly Val Leu Ser Met Asp Ser 50 55 60

Ser Asn Val Leu Gln Leu Ile Val Asp Ala Tyr Gly Lys Ile Arg Ser 65 70 75 80

Lys Val Glu Leu Glu Val Arg Asp Leu Pro 85 90

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<220>

<221> CDS

<222> (1)..(417)

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130588.00025.ST25.txt

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ccc	att	aac	atc	tac	tat	cta	ata	gat	tta	agt	tac	agt	atq	aaa	gat	
96	_							_		_			Met			
		P	·20	-1-	-1-			25			- 1		30		r	
															•	
gat 44	tta	tgg	agt	ata	cag	aat	ttg	999	acc	aag	ctt	gca	acc	caa	atg	1
	Leu	Trp	Ser	Ile	Gln	Asn	Leu	Gly	Thr	Lys	Leu	Ala	Thr	Gln	Met	
		35					40					45				
202	220	ata	202	tca	220	tta	3.aa	att	aas	+++	aas	aca	ttc	att	cat	1
92													Phe			,
AIG	_	neu	T11 T	Ser	ASII	55	nr 9	TYC	.:	rne	60	ALU	1110	vai	чор	
	50					55					00					
aag 40	cct	gtg	tca	ccg	tat	atg	tac	atc _.	tct	ccc	cca	gag	gct	tta	gaa	2
	Pro	Val	Ser	Pro	Tyr	Met	Tyr	Ile	Ser	Pro	Pro	Glu	Ala	Leu	Glu	
65					70					75					80	
224	000	tat	tad	asa	ata	222		202	'tat	tta	act	ato	ttt	aat	tat	2
88	_			-									Phe			2
ASII	PIO	Cys	тАт	85	Mec	пуъ	TIIT	7117	90	neu	FIO	Met	FILE	95	1 Y T	
				65					90					93		
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36 Lys	His	Val	Leu	Thr	Leu	Thr	Asp	Gln	Val	Thr	Arg	Phe	Asn	Glu	Glu	

105

100

110

130588.00025.ST25.txt

3

4

gtc aag aaa cag agc gtg tcc cgg aac cgc gat gcg cca gag ggc gga

Val Lys Lys Gln Ser Val Ser Arg Asn Arg Asp Ala Pro Glu Gly Gly

115 120 125

ttc gac gcc ata atg caa gca act gtc tgc gat

Phe Asp Ala Ile Met Gln Ala Thr Val Cys Asp

130 135

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1 5 10 15

Pro Val Asp Ile Tyr Tyr Leu Met Asp Leu Ser Tyr Ser Met Lys Asp.
20 25 30

Asp Leu Trp Ser Ile Gln Asn Leu Gly Thr Lys Leu Ala Thr Gln Met 35 40 45

Arg Lys Leu Thr Ser Asn Leu Arg Ile Gly Phe Gly Ala Phe Val Asp 50 55 60

Lys Pro Val Ser Pro Tyr Met Tyr Ile Ser Pro Pro Glu Ala Leu Glu 65 70 75 80

Asn Pro Cys Tyr Asp Met Lys Thr Thr Cys Leu Pro Met Phe Gly Tyr 85 90 95

130588.00025.ST25.txt

Lys His Val Leu Thr Leu Thr Asp Gln Val Thr Arg Phe Asn Glu Glu
100 105 110

Val Lys Lys Gln Ser Val Ser Arg Asn Arg Asp Ala Pro Glu Gly Gly 115 120 125

Phe Asp Ala Ile Met Gln Ala Thr Val Cys Asp 130 135

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<211> 117

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<222> (1)..(117)

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Tyr Met Tyr Ile Ser Pro Pro Glu Ala Leu Glu Asn Pro Cys Tyr Asp

1 5 10 15

atg aaa act acc tgc tta cca atg ttt gga tat aag cat gta tta aca 96 Met Lys Thr Thr Cys Leu Pro Met Phe Gly Tyr Lys His Val Leu Thr

20 25 30

tta acg gac caa gta aca aga 17

Leu Thr Asp Gln Val Thr Arg

35

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<211> 6 <212> PRT

177

130588.00025.ST25.txt

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<210> 175
<211> 39
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Integrin
<400>
      175
Tyr Met Tyr Ile Ser Pro Pro Glu Ala Leu Glu Asn Pro Cys Tyr Asp
                                                         15
Met Lys Thr Thr Cys Leu Pro Met Phe Gly Tyr Lys His Val Leu Thr
            20
                                25
Leu Thr Asp Gln Val Thr Arg
        35
<210> 176
<211> 18
<212> DNA
<213> Artificial Sequence
<220>
<223>
      Description of Artificial Sequence: Integrin
<220>
<221>
      CDS
      (1)..(18)
<222>
<400> 176
aga aat aga gat gca tat
Arg Asn Arg Asp Ala Tyr
1
                5
```

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```
130588.00025.ST25.txt
       Artificial Sequence
<213>
<220>
       Description of Artificial Sequence: Integrin
<223>
       177
<400>
Arq Asn Arg Asp Ala Tyr
       178
<210>
<211>
       48
<212>
      DNA
       Artificial Sequence
<213>
<220>
<223> Description of Artificial Sequence: Integrin
<220>
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       CDS
      (1)..(48)
<222>
<400>
       178
gac gca cca gaa gga gga ttt gat gca ata atg caa gca aca gta tat
Asp Ala Pro Glu Gly Gly Phe Asp Ala Ile Met Gln Ala Thr Val Tyr
                5
                                    10
                                                         15
1
       179
<210>
<211>
      16
<212>
      PRT
<213> Artificial Sequence
<220>
      Description of Artificial Sequence: Integrin
<223>
<400>
       179
Asp Ala Pro Glu Gly Gly Phe Asp Ala Ile Met Gln Ala Thr Val Tyr
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<210> 180

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130588.00025.ST25.txt
       24
<211>
       DNA
<212>
       Artificial Sequence
<213>
<220>
       Description of Artificial Sequence: Integrin
<223>
<220'>
       CDS
<221>
· <222>
      (1)..(24)
<400>
       180
tgc tat gat atg aaa aca aca tgt
Cys Tyr Asp Met Lys Thr Thr Cys
                5
1
<210> 181
<211>
<212> PRT
<213> Artificial Sequence
<220>
       Description of Artificial Sequence: Integrin
<223>
       181
<400>
Cys Tyr Asp Met Lys Thr Thr Cys
<210> 182
      60
<211>
<212>
      DNA
<213> Artificial Sequence
<220>
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<223>
<220>
<221>
      CDS
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<222> (1)..(60)

130588.00025.ST25.txt

<400> 182
aat ttt agt ata cag gta aga caa gta gaa gac tat cca gta gat ata
48
Asn Phe Ser Ile Gln Val Arg Gln Val Glu Asp Tyr Pro Val Asp Ile
1 5 10 15

tat tac tta atg 60 Tyr Tyr Leu Met

20

<210> 183
<211> 20
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Integrin

Asn Phe Ser Ile Gln Val Arg Gln Val Glu Asp Tyr Pro Val Asp Ile 1 5 10 15

Tyr Tyr Leu Met 20

<210> 184 <211> 15

<400> 183

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Integrin

<220>

<221> CDS

<222> (1)..(15)

<400> 184

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130588.00025.ST25.txt
gat atg aaa aca aca
15
Asp Met Lys Thr Thr
1
                5
<210> 185
<211> 5
<212> PRT
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Integrin
<400> 185
Asp Met Lys Thr Thr
<210> 186
<211> 15
<212> DNA
<213> Artificial Sequence
<220>
<223> Description of Artificial Sequence: Integrin
<220>
<221> CDS
<222> (1)..(15)
<400> 186
ata agt cca cca gca
15
Ile Ser Pro Pro Ala
                5
1
<210> 187
```

<210> 187 <211> 5 <212> PRT <213> Artificial Sequence

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<220>
      Description of Artificial Sequence: Integrin
<223>
      187
<400>
Ile Ser Pro Pro Ala
                5
      188
<210>
      36
<211>
<212> DNA
<213> Artificial Sequence
<220>
      Description of Artificial Sequence: Integrin
<223>
<220>
<221> CDS
      (1)..(36)
<222>
      188
<400>
aaa caa agt gta agt aga aat aga gat gca cca gaa
36
Lys Gln Ser Val Ser Arg Asn Arg Asp Ala Pro Glu
                                    10
                5
1
<210> 189
<211>
      12
<212> PRT ·
<213> Artificial Sequence
            . 1
<220>
      Description of Artificial Sequence: Integrin
<223>
<400>
      189
Lys Gln Ser Val Ser Arg Asn Arg Asp Ala Pro Glu
                                    10
                5
1
<210>
      190
<211>
      837
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<212> DNA Artificial Sequence <213> <220> Description of Artificial Sequence: Integrin <223> <220> CDS <221> (1)..(837)<222> <400> 190 gat gac agt aaa aat ttt agt atc cag gta aga cag gta gaa gat tat Asp Asp Ser Lys Asn Phe Ser Ile Gln Val Arg Gln Val Glu Asp Tyr 10 15 5 1 cca qtc gac ata tat tac ctc atg gac ctg agt tac agt atg aag gat 96 Pro Val Asp Ile Tyr Tyr Leu Met Asp Leu Ser Tyr Ser Met Lys Asp 30 25 2.0 gat ctc tgg tca att caa aat cta ggg act aag ctt gcg acg caa atg 1 Asp Leu Trp Ser Ile Gln Asn Leu Gly Thr Lys Leu Ala Thr Gln Met 40 45 35 aga aaa ttg aca agc aat tta cga att gga ttt gga gca ttc gtc gat 1 Arg Lys Leu Thr Ser Asn Leu Arg Ile Gly Phe Gly Ala Phe Val Asp 55 60 50 aag cet gtt agt eet tae atg tae ate tea eee eet gaa gee tta gag 2 Lys Pro Val Ser Pro Tyr Met Tyr Ile Ser Pro Pro Glu Ala Leu Glu 70 75 80 65 aac ccc tgc tat gac atg aaa acc aca tgt tta ccg atg ttt ggt tat 2

Page 128

130588.00025.ST25.txt Asn Pro Cys Tyr Asp Met Lys Thr Thr Cys Leu Pro Met Phe Gly Tyr aaa cat gtg ctc acg ctt acg gac caa gtg act cgg ttc aat gag gaa Lys His Val Leu Thr Leu Thr Asp Gln Val Thr Arq Phe Asn Glu Glu gta aaa aag cag tot gto agt agg aac cgt gat gca ccg gaa gga gga Val Lys Lys Gln Ser Val Ser Arg Asn Arg Asp Ala Pro Glu Gly Gly ttt qac qcq ata atg caa gcc aca gta tgt gac gag aaa ata qqc tgq Phe Asp Ala Ile Met Gln Ala Thr Val Cys Asp Glu Lys Ile Gly Trp cgc aac gat gca tcc cat tta ctg gtg ttc acc act gat qcq aaa aca Arg Asn Asp Ala Ser His Leu Leu Val Phe Thr Thr Asp Ala Lys Thr cac atc gca ttg gat ggt aga ttg gct gga ata gta cag cca aat gat His Ile Ala Leu Asp Gly Arg Leu Ala Gly Ile Val Gln Pro Asn Asp ggc caa tqc cat gtc ggg agc gac aac cac tat tcg gca aqt acc acq Gly Gln Cys His Val Gly Ser Asp Asn His Tyr Ser Ala Ser Thr Thr

130588.00025.ST25.txt atg gac tac ccc age tta ggt cta atg act gag aag tta tcg cag aag 6 Met Asp Tyr Pro Ser Leu Gly Leu Met Thr Glu Lys Leu Ser Gln Lys 205 200 195 aac ctt aac cta atc ttc gct gta aca gaa aat gta gtt aat tta tat 6 Asn Leu Asn Leu Ile Phe Ala Val Thr Glu Asn Val Val Asn Leu Tyr 220 215 210 caa aac tac tcg gaa ctg ata ccg gga aca aca gtt ggg gtc ttg tcc 7 20 Gln Asn Tyr Ser Glu Leu Ile Pro Gly Thr Thr Val Gly Val Leu Ser 240 230 235 225 1 atq gac tca agt aat gtt tta cag cta att gtg gac gct tat ggc aag Met Asp Ser Ser Asn Val Leu Gln Leu Ile Val Asp Ala Tyr Gly Lys 255 245 250 att aga tcc aaa gtg gag tta gaa gtt aga gat ctt cca gag gag ctc Ile Arg Ser Lys Val Glu Leu Glu Val Arg Asp Leu Pro Glu Glu Leu 270 260 265 8 tct ctq tct ttt aac gcc acc Ser Leu Ser Phe Asn Ala Thr 275

<210> 191 <211> 279 <212> PRT <213> Artificial Sequence

130588.00025.ST25.txt

<220>

<223> Description of Artificial Sequence: Integrin

<400> 191

Pro Val Asp Ile Tyr Tyr Leu Met Asp Leu Ser Tyr Ser Met Lys Asp 20 25 30

Asp Leu Trp Ser Ile Gln Asn Leu Gly Thr Lys Leu Ala Thr Gln Met 35 40 45

Arg Lys Leu Thr Ser Asn Leu Arg Ile Gly Phe Gly Ala Phe Val Asp 50 55 60

Lys Pro Val Ser Pro Tyr Met Tyr Ile Ser Pro Pro Glu Ala Leu Glu 65 70 75 80

Asn Pro Cys Tyr Asp Met Lys Thr Thr Cys Leu Pro Met Phe Gly Tyr 85 90 95

Lys His Val Leu Thr Leu Thr Asp Gln Val Thr Arg Phe Asn Glu Glu 100 105 110

Val Lys Lys Gln Ser Val Ser Arg Asn Arg Asp Ala Pro Glu Gly Gly 115 120 125

Phe Asp Ala Ile Met Gln Ala Thr Val Cys Asp Glu Lys Ile Gly Trp 130 135 140

Arg Asn Asp Ala Ser His Leu Leu Val Phe Thr Thr Asp Ala Lys Thr 145 150 155 160

His Ile Ala Leu Asp Gly Arg Leu Ala Gly Ile Val Gln Pro Asn Asp 165 170 175

Gly Gln Cys His Val Gly Ser Asp Asn His Tyr Ser Ala Ser Thr Thr 180 185 190

Met Asp Tyr Pro Ser Leu Gly Leu Met Thr Glu Lys Leu Ser Gln Lys 195 200 205

Asn Leu Asn Leu Ile Phe Ala Val Thr Glu Asn Val Val Asn Leu Tyr 210 215 220

Gln Asn Tyr Ser Glu Leu Ile Pro Gly Thr Thr Val Gly Val Leu Ser 225 230 235 240

Met Asp Ser Ser Asn Val Leu Gln Leu Ile Val Asp Ala Tyr Gly Lys 245 250 255

Ile Arg Ser Lys Val Glu Leu Glu Val Arg Asp Leu Pro Glu Glu Leu 260 265 270

Ser Leu Ser Phe Asn Ala Thr 275

<210> 192

<211> 621

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Integrin

<220>

<221> CDS

<222> (1)..(621)

<400> 192

gat gat tot aag aat tit too ato oag git oga oag git gaa gat tao

Asp Asp Ser Lys Asn Phe Ser Ile Gln Val Arg Gln Val Glu Asp Tyr

1 5 10 15

130588.00025.ST25.txt

сса 96	gta	gac	ata	tat	tac	cta	atg	gat	ctc	agt	tat	agt [°]	atg	aag	gac	
	Val	Asp	Ile	Tyr	Tyr	Leu	Met	Asp	Leu	Ser	Tyr	Ser	Met	Lys	Asp	
			20					25					30			
gat 44	cta	tgg	agt	atc	caa	aac	ctg	ggc	acg	aaa	ctt	gcc	act	caa	atg	1
	Leu	Trp	Ser	Ile	Gln	Asn	Leu	Gly	Thr	Lys	Leu	Ala	Thr	Gln	Met	
		35					40					45				
cgg 92	aaa	tta	aca	tca	aac	ttg	agg	att	ggc	ttt	999	gca	ttc	gtg	gat	1
Arg	Lys	Leu	Thr	Ser	Asn	Leu	Arg	Ile	Gly	Phe	Gly	Ala	Phe	Val	Asp	
	50					55					60					
												•				
aaa 40	CCC	gta	tcc	сса	tat	atg	tac	atc	tct	cca	ccg	gag	gca	ctc	gaa	2
	Pro	Val	Ser	Pro	Tyr	Met	Tyr	Ile	Ser	Pro	Pro	Glu	Ala	Leu	Glu	
65					70					75					80	
aac 88	cct	tgc	tac	gac	atg	aag	acc	aca	tgc	ctt	cct	atg	ttt	999	tat	2
	Pro	Cys	Tyr	Asp	Met	Lys	Thr	Thr	Cys	Leu	Pro	Met	Phe	Gly	Tyr	
				85					90					95		
aaa 36	cac	gtg	ctt	act	tta	acc	gac	cag	gtt	acg	aga	ttc	aat	gaa	gag	3
	His	Val	Leu	Thr	Leu	Thr	qaA	Gln	Val	Thr	Arg	Phe	Aśn	Glu	Glu	
			100					105					110			•
								•								
_	aaa	aag	caa	agt	gta	agc	cgt	aac	aga	gac	gca	ccg.	gag	gga	999	3
84 Val	Lys	Lys	Gln	Ser	Val	Ser	Arg	Asn	Arg	Asp	Ala	Pro	Glu	Gly	Gly	

. *		115	,		-	130	588. 120	0002	5.ST	хt	125					
32	gac	_														4
Phe	Asp	Ala	IIe	Met	GIn		Thr	val	Cys	Asp		ьуѕ	TTE	GIY	irp	
	130					135					140					
80	aat											•				4
Arg	Asn	Asp	Ala	Ser	His	Leu	Leu	Val	Phe	Thr	Thr	Asp	Ala	Lys	Thr	
145			•		150					155					160	
63.0	att	aca	cta	asc	aat	cac	ctc	gca	aac	ata	at.t.	cag	сса	aat	gat	5
28																
HIS	TTE	Ala	пеп		GIY	Arg	лец	ALG		110	val	0111	110		пор	
				100					170					173		
	cag	tgt	cat	gtg	ggt	agt	gat	aat	cat	tat	agc	gct	tca	aca	acc	5
76 Gly	Gln	Cys	His	Val	Gly	Ser	Asp	Asn	His	Tyr	Ser	Ala	Ser	Thr	Thr	
			180					185					190			
			-													_
21			•													
Met	Asp	Tyr	Pro	Ser	Leu	Gly	Leu	Met	Thr	Glu	Lys	Leu	Ser	Gln		
		195					200	•				205				
<21 <21 <21 <21	1> 2 2> 3	193 207 PRT Arti:	ficia	al Se	equei	nce						·				
His ggt 76 Gly atg 21 Met <21 <21 <21	Gln gac Asp	tgt Cys tac Tyr 195 193 207 PRT	cat His 180 ccc Pro	gtg Val agt Ser	ggt Gly cta Leu	agt Ser gga Gly	gat Asp ctg Leu	aat Asn 185 atg Met	170 cat His	tat Tyr gaa	agc Ser aag	gct Ala ttg Leu	tca Ser 190 tcg	175 aca Thr	acc	

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<223> Description of Artificial Sequence: Integrin

<220>

<400>

193

Asp	Asp	Ser	Lys	Asn	Phe	Ser	Ile	Gln	Val	Arg	Gln	Val	Glu	Asp	Tyr
1	_			5					10					15	

Pro Val Asp Ile Tyr Tyr Leu Met Asp Leu Ser Tyr Ser Met Lys Asp
20 25 30

Asp Leu Trp Ser Ile Gln Asn Leu Gly Thr Lys Leu Ala Thr Gln Met 35 40 45

Arg Lys Leu Thr Ser Asn Leu Arg Ile Gly Phe Gly Ala Phe Val Asp 50 55 60

Lys Pro Val Ser Pro Tyr Met Tyr Ile Ser Pro Pro Glu Ala Leu Glu 65 70 75 80

Asn Pro Cys Tyr Asp Met Lys Thr Thr Cys Leu Pro Met Phe Gly Tyr 85 90 95

Lys His Val Leu Thr Leu Thr Asp Gln Val Thr Arg Phe Asn Glu Glu
100 105 110

Val Lys Lys Gln Ser Val Ser Arg Asn Arg Asp Ala Pro Glu Gly Gly
115 120 125

Phe Asp Ala Ile Met Gln Ala Thr Val Cys Asp Glu Lys Ile Gly Trp 130 135 140

Arg Asn Asp Ala Ser His Leu Leu Val Phe Thr Thr Asp Ala Lys Thr 145 150 155 160

His Ile Ala Leu Asp Gly Arg Leu Ala Gly Ile Val Gln Pro Asn Asp 165 170 175

Gly Gln Cys His Val Gly Ser Asp Asn His Tyr Ser Ala Ser Thr Thr 180 185 190

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Met Asp Tyr Pro Ser Leu Gly Leu Met Thr Glu Lys Leu Ser Gln 195 200 205

<210> 194

<211> 1053

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Integrin

<220>

<221> CDS

<222> (1)..(1053)

<400> 194

aag caa ctg aat ttc acg gcc tct gga gag gca gag gcc cgc aga tgc

Lys Gln Leu Asn Phe Thr Ala Ser Gly Glu Ala Glu Ala Arg Arg Cys

1 5 10 15

gca cgg agg gaa gag ctc cta gct agg gga tgc ccc ctg gag gag cta 96 Ala Arg Arg Glu Glu Leu Leu Ala Arg Gly Cys Pro Leu Glu Glu Leu

20 25 30

gaa gag cca cgt gga cag caa gag gta cta cag gat cag ccg ctg tcg 1 44 Glu Glu Pro Arg Gly Gln Gln Glu Val Leu Gln Asp Gln Pro Leu Ser

35 40 45

caa gga gcc cga ggt gag ggt gcg acc cag cta gca cca caa cgc gta 192 Gln Gly Ala Arg Gly Glu Gly Ala Thr Gln Leu Ala Pro Gln Arg Val

55 . 60

cgc gtt aca tta cgg cca ggc gaa cca caa caa tta cag gta aga ttt 2

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130588.00025.ST25.txt

40 Arg	Val	Thr	Leu	Arg	Pro	Gly	Glu	Pro	Gln	Gln	Leu	Gln	Val	Arg	Phe	
65					70					75					80	
	cgt	gct	gaa	999	tat	ccg	gtg	gat	tta	tac	tat	ctc	atg	gat	ctt	2,
88 Leu	Arg	Ala	Glu	Gly	Tyr	Pro	Val	Asp	Leu	Tyr	Tyr	Leu	Met	Asp	Leu	
				85					90					95		
agt 36	tac	tcc	atg	aag	gat	gat	cta	gaa	agg	gta	cgc	caa	ctg	ggt	cat	3
Ser	Tyr	Ser	Met	Lys	Asp	Asp	Leu	Glu	Arg	Val	Arg	Gln	Leu	Gly	His	
			100					105					110			
_	tta	ttg	gta	aga	tta	caa	gaa	gta	aca	cat	agc	gta	cgt	atc	9 99	3
84 Ala	Leu	Leu	Val	Arg	Leu	Gln	Glu	Val	Thr	His	Ser	Val	Arg	Ile	Gly	
	·	115					120					125				
ttt 32	gga	tct	ttc	gta	gac	aaa	acc	gtt	tta	cct	ttc	gtg	agt	acc	gtg	4
Phe	Gly	Ser	Phe	Val	Asp	Lys	Thr	Val	Leu	Pro	Phe	Val	Ser	Thr	Val	
	130					135					140					
	agc	aaa	ttg	cgt	cac	cct	tgt	cca	act	agg	ctt	gag	cga	tgc	cag	4
80 Pro	Ser	Lys	Leu	Arg	His	Pro	Cys	Pro	Thr	Arg	Leu	Glu	Arg	Cys	Gln	
145					150					155					160	
_	ccg	ttc	tca	ttc	cac	cat	gtt	ttg	agt	tta	act	gga	gat	gcc	cag	5
28 Ser	Pro	Phe	Ser	Phe	His	His	Val	Leu	Ser	Leu	Thr	Gly	Asp	Àla	Gln	
				165					170					175		

130588.00025.ST25.txt gcc ttc qag cga gaa gtc ggc cgg caa tcc gtt tct ggg aat tta gac Ala Phe Glu Arg Glu Val Gly Arg Gln Ser Val Ser Gly Asn Leu Asp agt ccc gag gga ggg ttt gac gcg ata ctt caa gca gcg ctc tgt caq Ser Pro Glu Gly Gly Phe Asp Ala Ile Leu Gln Ala Ala Leu Cys Gln gaa cag att ggc tgg cga aac gtc agc aga cta tta gtc ttt acq agt Glu Gln Ile Gly Trp Arg Asn Val Ser Arg Leu Leu Val Phe Thr Ser gac gat act ttt cac aca gca ggg gac gga aag ctt ggc ggt att ttt Asp Asp Thr Phe His Thr Ala Gly Asp Gly Lys Leu Gly Gly Ile Phe atq ccc agc gac ggt cat tgt cac ctc gat tca aat gga ttg tac agt Met Pro Ser Asp Gly His Cys His Leu Asp Ser Asn Gly Leu Tyr Ser cqq tcc aca qaa ttc qat tat cct tcq gtq qqc cag gtg gcg cag gca Arg Ser Thr Glu Phe Asp. Tyr Pro Ser Val Gly Gln Val Ala Gln Ala ctq aqt qct qca aac atc caq cca ata ttt qct qtt aca tcq gcg gcq Leu Ser Ala Ala Asn Ile Gln Pro Ile Phe Ala Val Thr Ser Ala Ala

130588.00025.ST25.txt

					-											
_	ccg	gtt	tac	caa	gaa	ctc	tca	aaa	tta	ata	CCC	aaa	tcc	gct	gtc	9
12 Leu	Pro	Val	Tyr	Gln	Glu	Leu	Ser	Lys	Leu	Ile	Pro	Lys	Ser	Ala	Val	
	290					295					300					,
	gaa	tta	tct	gag	gac	tcc	tca	aac	gtg	gtc	caa	ctc	atc	atg	gac	9
60 Gly	Glu	Leu	Ser	Glu	Asp	Ser	Ser	Asn	Val	Val	Gln	Leu	Ile	Met	Asp	
305					310					315					320	·.
-	tat	aat	tcg	ctt	agt	agc	acg	gta	aca	ctg	gaa	cac	tca	tcg	ctt	10
08 Ala	Tyr	Asn	Ser	Leu	Ser	Ser	Thr	Val	Thr	Leu	Glu	His	Ser	Ser	Leu	
				325					330			-		335		
_	ccc	ggt	gtc	cat	att	tct	tat	gag	agt	caa	tgt	gaa	ggg	cct		10
53 Pro	Pro	Gly	Val	His	Ile	Ser	Tyr	Glu	Ser	Gln	Cys	Glu	Gly	Pro		
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<210> 195

<211> 351

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Integrin

<400> 195

Lys Gln Leu Asn Phe Thr Ala Ser Gly Glu Ala Glu Ala Arg Arg Cys 1 5 10 15

Ala Arg Arg Glu Glu Leu Leu Ala Arg Gly Cys Pro Leu Glu Glu Leu 20 25 30

130588.00025.ST25.txt

Glu Glu Pro Arg Gly Gln Gln Glu Val Leu Gln Asp Gln Pro Leu Ser 35 40 45

- Gln Gly Ala Arg Gly Glu Gly Ala Thr Gln Leu Ala Pro Gln Arg Val 50 55 60
- Arg Val Thr Leu Arg Pro Gly Glu Pro Gln Gln Leu Gln Val Arg Phe 65 70 75 80
- Leu Arg Ala Glu Gly Tyr Pro Val Asp Leu Tyr Tyr Leu Met Asp Leu 85 90 95
- Ser Tyr Ser Met Lys Asp Asp Leu Glu Arg Val Arg Gln Leu Gly His
 100 105 110
- Ala Leu Leu Val Arg Leu Gln Glu Val Thr His Ser Val Arg Ile Gly
 115 120 125
- Phe Gly Ser Phe Val Asp Lys Thr Val Leu Pro Phe Val Ser Thr Val 130 135 140
- Pro Ser Lys Leu Arg His Pro Cys Pro Thr Arg Leu Glu Arg Cys Gln 145 150 155 160
- Ser Pro Phe Ser Phe His His Val Leu Ser Leu Thr Gly Asp Ala Gln 165 170 175
- Ala Phe Glu Arg Glu Val Gly Arg Gln Ser Val Ser Gly Asn Leu Asp 180 185 190
- Ser Pro Glu Gly Gly Phe Asp Ala Ile Leu Gln Ala Ala Leu Cys Gln 195 200 205
- Glu Gln Ile Gly Trp Arg Asn Val Ser Arg Leu Leu Val Phe Thr Ser 210 215 220

Asp Asp Thr Phe His Thr Ala Gly Asp Gly Lys Leu Gly Gly Ile Phe 225 230 235 240

Met Pro Ser Asp Gly His Cys His Leu Asp Ser Asn Gly Leu Tyr Ser 245 250 255

Arg Ser Thr Glu Phe Asp Tyr Pro Ser Val Gly Gln Val Ala Gln Ala 260 265 270

Leu Ser Ala Ala Asn Ile Gln Pro Ile Phe Ala Val Thr Ser Ala Ala 275 280 285

Leu Pro Val Tyr Gln Glu Leu Ser Lys Leu Ile Pro Lys Ser Ala Val 290 295 300

Gly Glu Leu Ser Glu Asp Ser Ser Asn Val Val Gln Leu Ile Met Asp, 305 310 315 320

Ala Tyr Asn Ser Leu Ser Ser Thr Val Thr Leu Glu His Ser Ser Leu 325 330 335

Pro Pro Gly Val His Ile Ser Tyr Glu Ser Gln Cys Glu Gly Pro 340 345 350

<210> 196

<211> 273

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Integrin

<220>

<221> CDS

<222> (1)..(273)

<400> 196

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130588.00025.ST25.txt Ser Phe Val Asp Lys Thr Val Leu Pro Phe Val Ser Thr Val Pro Ser																	
Ser	Phe	Val	Asp	Lys	Thr	Val	Leu	Pro	Phe	Val	Ser	Thr	Val	Pro	Ser		
1				5					10					15			
												•					
aag 96	tta	cgc	cat	cca	tgt	cca	acg	agg	ttg	gag	aga	tgc	cag	tct	cet		
	Leu	Arg	His	Pro	Cys	Pro	Thr	Arg	Leu	Gļu	Arg	Cys	Gln	Ser	Pro		
			20		•			25					30				
ttt 44	tcc	ttc	cac	cat	gtc	tta	agc	cta	act	ggt	gac	gct	caa	gcc	ttt	1	
	Sèr	Phe	His	His	Val	Leu	Ser	Leu	Thr	Gly	Asp	Ala	Gln	Ala	Phe		
		35					40					45					
gaa 92	cgg	gaa	gta	gga	aga	caa	tcg	gtg	agt	999	aac	ctt	gat	tca	ccc	1	
Glu	Arg	Glu	Val	Gly	Arg	Ģln	Ser	Val	Ser	Gly	Asn	Leu	Asp	Ser	Pro		
	50					55					60						
											•						
gaa 40	gga	ggc	ttc	gac	gca	ata	tta	cag	gcg	gca	ctc	tgt	cag	gag	caa	2	
	Gly	Gly	Phe	Asp	Ala	Ile	Leu	Gln	Ala	Ala	Leu	Cys	Gln	Glu	Gln		
65					70					75					80		
ata 73	gga	tgg	cga	aat	gtt	agt	cgt	tta	tta	gtg						2	
	Gly	Trp	Arg	Asn	Val	Ser	Arg	Leu	Leu	Val							
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<220> <223> Description of Artificial Sequence: Integrin																	

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<400> 197

Ser Phe Val Asp Lys Thr Val Leu Pro Phe Val Ser Thr Val Pro Ser 1 5 10 15

Lys Leu Arg His Pro Cys Pro Thr Arg Leu Glu Arg Cys Gln Ser Pro 20 25 30

Phe Ser Phe His His Val Leu Ser Leu Thr Gly Asp Ala Gln Ala Phe 35 40 45

Glu Arg Glu Val Gly Arg Gln Ser Val Ser Gly Asn Leu Asp Ser Pro 50 55 60

Glu Gly Gly Phe Asp Ala Ile Leu Gln Ala Ala Leu Cys Gln Glu Gln 65 70 75 80

Ile Gly Trp Arg Asn Val Ser Arg Leu Leu Val 85 90

<210> 198

<211> 312

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Integrin

<220>

<221> CDS

<222> (1)..(312)

<400> 198

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1 5 10 15

130588.00025.ST25.txt

qcc agg cga gaa gaa tta ttg gca cgc ggg tgt ccc ctg gag gag ctt Ala Arq Arg Glu Glu Leu Leu Ala Arg Gly Cys Pro Leu Glu Glu Leu

> 30 25 20

gaa gag cca cgg ggt cag cag gaa gtt tta caa gat caa cca tta agt 1 Glu Glu Pro Arg Gly Gln Gln Glu Val Leu Gln Asp Gln Pro Leu Ser 45 35 40

cag gga gca cgc ggc gaa ggg gcg aca caa tta gcg cca cag cgt gtc 1 92 Gln Gly Ala Arg Gly Glu Gly Ala Thr Gln Leu Ala Pro Gln Arg Val 55 60 50

aga gtg aca ttg cga cca gga gag cct caa cag tta caa gta cgt ttt 2 Arg Val Thr Leu Arg Pro Gly Glu Pro Gln Gln Leu Gln Val Arg Phe 70 75 80

ctt cgg gcc gag ggt tac ccg gta gat ctg tac tac cta atg gac ctc 2 Leu Arg Ala Glu Gly Tyr Pro Val Asp Leu Tyr Tyr Leu Met Asp Leu 85 90 95

3 agt tat agt atg aag gac gat cta Ser Tyr Ser Met Lys Asp Asp Leu

100

65

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130588.00025.ST25.txt

<220>

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1 10 15

Ala Arg Arg Glu Glu Leu Leu Ala Arg Gly Cys Pro Leu Glu Glu Leu 20 25 30

Glu Glu Pro Arg Gly Gln Gln Glu Val Leu Gln Asp Gln Pro Leu Ser 35 40 45

Gln Gly Ala Arg Gly Glu Gly Ala Thr Gln Leu Ala Pro Gln Arg Val 50 55 60

Arg Val Thr Leu Arg Pro Gly Glu Pro Gln Gln Leu Gln Val Arg Phe 65 70 75 80

Leu Arg Ala Glu Gly Tyr Pro Val Asp Leu Tyr Tyr Leu Met Asp Leu 85 90 95

Ser Tyr Ser Met Lys Asp Asp Leu 100

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<211> 1017

<212> DNA

<213> Artificial Sequence

<220>

<223>. Description of Artificial Sequence: Integrin

<220>

<221> CDS

<222> (1)..(1017)

<400> 200

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Glu Lys Arg Glu Gly Lys Ala Glu Asp Arg Gly Gln Cys Asn His Val agg ata aac caa acc gta acc ttc tgg gtc tcg ctt cag gca act cat Arg Ile Asn Gln Thr Val Thr Phe Trp Val Ser Leu Gln Ala Thr His tgt tta ccc gaa cca cat ttg cta cgc ctc cgg gct tta ggg ttt tct Cys Leu Pro Glu Pro His Leu Leu Arg Leu Arg Ala Leu Gly Phe Ser gag gag ctc ata gtt gag cta cac acg tta tgt gac tgc aat tgc tca Glu Glu Leu Ile Val Glu Leu His Thr Leu Cys Asp Cys Asn Cys Ser gac acg caa cca caa gcg cca cac tgt tcc gat ggg cag ggg cac ctt Asp Thr Gln Pro Gln Ala Pro His Cys Ser Asp Gly Gln Gly His Leu caa tgt gga gtc tgt agt tgc gct cct ggt aga ttg ggt agg ctg tgc Gln Cys Gly Val Cys Ser Cys Ala Pro Gly Arg Leu Cys 90 . gag tgc agt gta gct gag tta tcg agt cct gat ctc gaa agc gga tgt Glu Cys Ser Val Ala Glu Leu Ser Ser Pro Asp Leu Glu Ser Gly Cys

													1 (1/(32003	/030/03	
						130	588.	0002	.5.SI		xt.					
cgc 84	gcg	ccg	aat	999	act	gga	cct	ctg	tgt	tcc	gga	aaa	999	cat	tgc	3
	Ala	Pro	Asn	Gly	Thr	Gly	Pro	Leu	Cys	Ser	Gly	Lys	Gly	His	Cys	
		115					120	-				125				
				1	12-	1				1					,	4
32							,					ggc -				4
Gln	Cys	Gly	Arg	Cys	Ser	Суѕ	Ser	Gly	Gln	Ser	Ser	Gly	His	Leu	Cys	
	130					135					140					
gaa	tat	gac	gac	acc	aqc	tqt	qaa	caa	cat	qaq	aac	att	ttq	tac	aaa	4
80			_												Gly.	
145	Cyb	1100	1100	,,,,,	150	<i>-</i> 1 <i>-</i> 2	 u	5		155	<i>0-1</i> .		200	O _J D	160	
143					100				•	133					100	
	ttc	ggc	agg	tgc	cag	tgt	999	gtg	tgt	cac	tgt	cat	gca	aac	cga	5
28 Gly	Phe	Gly	Arg	Cys	Gln	Cys	Gly	Val	Cys	His	Cys	His	Ala	Asn	Arg	
				165					170					175		
										•						
aca 76	ggt	cga	gca	tgc	gag	tgt	tcc	ggc	gac	atg	gat	tct	tgt	ata	agt	5
Thr	Gly	Arg	Ala	Cys	Glu	Cys	Ser	Gly	Asp	Met	qaA	Ser	Cys	Ile	Ser	
			180					185					190			٠
G.G.G		aas	cat	++-	taa	act	aat.	ant	gga	202	taa	226	taa	22+		6
24									_			aag	-		_	J
Pro	GIU		GIÀ	ьeu	CAR	ser		His	GTÀ	Arg	Cys	Lys	Сув	Asn	Arg	
		195		•			200					205	•			
tgc	caa	tgc	tta	gat	ggt	tac	tac	ggc	gcc	cta	tgt	gat	cag	tgc	cca	6
72	6 7	_	_	_	~ -	77 1	m-		7 7	~	~	_	~7	-		

220

Cys Gln Cys Leu Asp Gly Tyr Tyr Gly Ala Leu Cys Asp Gln Cys Pro

215

210

ggc 20	tgt	aag	act	cca	tgt	gaa	aga	cac	cga	gac	tgc	gca	gag	tgc	ggt	7
	Cys	Lys	Thr	Pro	Cys	Glu	Arg	His	Arg	Asp	Cys	Ala	Glu	Cys	Gly	
225					230					235					240	
gcg 68	ttt	aga	aca	ggc	ccc	ctg	gcc	acc	aat	tgc	agc	aca	gct	tgt	gct	7
	Phe	Arg	Thr	Gly	Pro	Leu	Ala	Thr	Asn	Cys	Ser	Thr	Ala	Cys	Ala	
				245					250					255		
cac 16	act	aat	gtg	acg	ctt	gca	ctt	gcg	ccc	ata	tta	gat	gac	ggc	tgg	8
	Thr	Asn	Val	Thr	Leu	Ala	Leu	Ala	Pro	Ile	Leu	Asp	Asp	Gly	Trp	
			260					265					270			
tgt 64	aaa	gaa	aga	aca	ttg	gat	aac	caa	ctg	ttt	ttt	ttc	cta	gta	gaa	8
	Lys.	Glu	Arg	Thr	Leu	Asp	Asn	Gln	Leu	Phe	Phe	Phe	Leu	Val	Glu	
		275					280					285				
gac 12	gat	gcc	aga	ggc	acg	gta	gtt	ctc	cgt	gtt	aga	ccg	caa	gaa	aag	9
	Asp	Ala	Arg	Gly	Thr	Val	Val	Leu	Arg	Val	Arg	Pro	Gln	Glu	Lys	
	290	٠				295		-			300					
gga 60	gca	gat	cat	acc	caa	gca	att	gta	ctg	999	tgt	gtt	999	gga	atc	9
	Ala	Asp	His	Thr	Gln	Ala	Ile	Val	Leu	Gly	Cys	Val	Gly	Gly	Ile	
305					310					315					320	
gtc 08	gca	gtg	999	cta	aga	ctc	gta	ctt	gcg	tat	cgt	ťta	tca	gtc	gaa	10
	Ala	Val	Gly	Leu	Gly	Leu	Val	Leu	Ala	Tyr	Arg	Leu	Ser	Val	Glu	
				325					330					335		

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10 atc tat gat 17 Ile Tyr Asp <210> 201 <211> 339 <212> PRTArtificial Sequence <213> <220> Description of Artificial Sequence: Integrin <223> 201 <400> Glu Lys Arg Glu Gly Lys Ala Glu Asp Arg Gly Gln Cys Asn His Val 10 Arg Ile Asn Gln Thr Val Thr Phe Trp Val Ser Leu Gln Ala Thr His 25 20 Cys Leu Pro Glu Pro His Leu Leu Arg Leu Arg Ala Leu Gly Phe Ser 40 35 Glu Glu Leu Ile Val Glu Leu His Thr Leu Cys Asp Cys Asn Cys Ser 60 55 50 Asp Thr Gln Pro Gln Ala Pro His Cys Ser Asp Gly Gln Gly His Leu 75 70 65 Gln Cys Gly Val Cys Ser Cys Ala Pro Gly Arg Leu Gly Arg Leu Cys 95 90 85 Glu Cys Ser Val Ala Glu Leu Ser Ser Pro Asp Leu Glu Ser Gly Cys

105

100

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Arg Ala Pro Asn Gly Thr Gly Pro Leu Cys Ser Gly Lys Gly His Cys 115 120 125

Gln Cys Gly Arg Cys Ser Cys Ser Gly Gln Ser Ser Gly His Leu Cys 130 135 140

Glu Cys Asp Asp Ala Ser Cys Glu Arg His Glu Gly Ile Leu Cys Gly 145 150 155 160

Gly Phe Gly Arg Cys Gln Cys Gly Val Cys His Cys His Ala Asn Arg 165 170 175

Thr Gly Arg Ala Cys Glu Cys Ser Gly Asp Met Asp Ser Cys Ile Ser 180 185 190

Pro Glu Gly Gly Leu Cys Ser Gly His Gly Arg Cys Lys Cys Asn Arg 195 200 205

Cys Gln Cys Leu Asp Gly Tyr Tyr Gly Ala Leu Cys Asp Gln Cys Pro 210 215 220

Gly Cys Lys Thr Pro Cys Glu Arg His Arg Asp Cys Ala Glu Cys Gly 225 230 235 240

Ala Phe Arg Thr Gly Pro Leu Ala Thr Asn Cys Ser Thr Ala Cys Ala 245 250 255

His Thr Asn Val Thr Leu Ala Leu Ala Pro Ile Leu Asp Asp Gly Trp 260 265 270

Cys Lys Glu Arg Thr Leu Asp Asn Gln Leu Phe Phe Leu Val Glu 275 280 285

Asp Asp Ala Arg Gly Thr Val Val Leu Arg Val Arg Pro Gln Glu Lys 290 295 300

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130588.00025.ST25.txt
Gly Ala Asp His Thr Glin Ala Ile Val Leu Gly Cys Val Gly Gly Ile
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                                         315
                    310
305
Val Ala Val Gly Leu Gly Leu Val Leu Ala Tyr Arg Leu Ser Val Glu
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                                     330
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Ile Tyr Asp
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1
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Glu His Ile Pro Ala
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130588.00025.ST25.txt

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48

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15 10 5 1

atg tta gca aga

Met Leu Ala Arg

20

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Artificial Sequence <213>

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Description of Artificial Sequence: Integrin <223>

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Met Leu Ala Arg

20

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<221> CDS

<222> (1)..(24)

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24
Cys Trp Asp Asp Gly Trp Leu Cys
                5
1
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Cys Trp Asp Asp Gly Trp Leu Cys
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24
Cys Trp Asp Asp Leu Trp Leu Cys
1
                5
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<211>
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      PRT
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130588.00025.ST25.txt
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       213
Cys Leu Leu Arg Met Arg Ser Ile Cys
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130588.00025.ST25.txt

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<213> Artificial Sequence

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Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His Gly

1 5 10 15

gta aca agt gct

60

Val Thr Ser Ala

20

<210> 215

<211> 20

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Integrin

<400> 215

Pro Asp Thr Arg Pro Ala Pro Gly Ser Thr Ala Pro Pro Ala His Gly
1 5 10 15

Val Thr Ser Ala 20

<210> 216

<211> 42 ·

130588.00025.ST25.txt

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42
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                5
1
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                                     10
                5
<210> 218
      18
<211>
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gaa tgg cca gag tat tta 18 Glu Trp Pro Glu Tyr Leu

1 5

<210> 219

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